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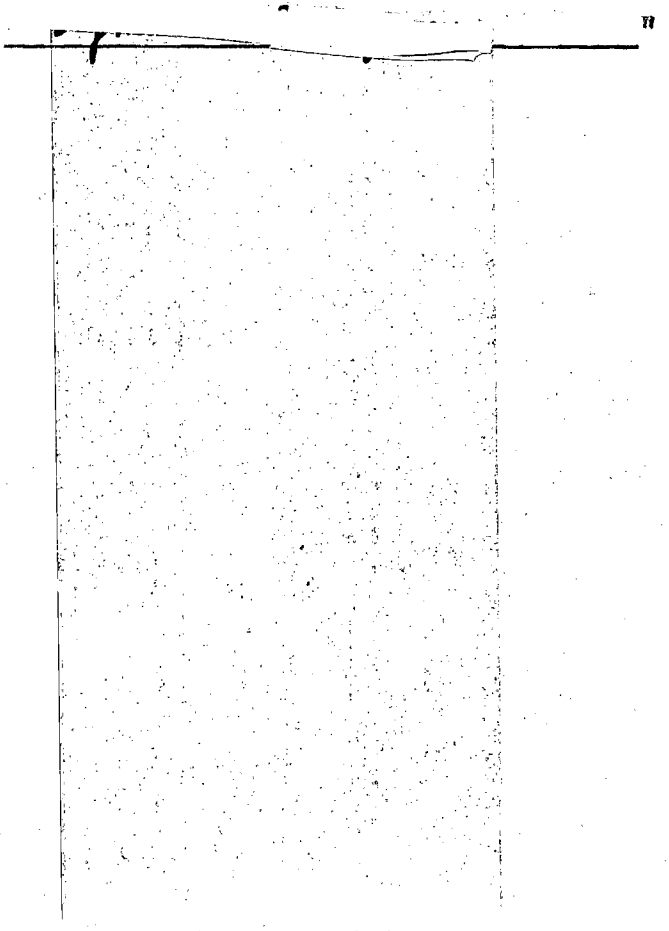

STUDIES OF RACEMIZATION RATES IN SOLVENTS OF INTERMEDIATE DIELECTRIC CONSTANT

A THESIS

Presented to

the Faculty of the Graduate Division

by

Lyman Wallace Morgan

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

in the School of Chemistry

Georgia Institute of Technology

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STUDIES OF RACEMIZATION RATES IN SOLVENTS OF INTERMEDIATE DIELECTRIC CONSTANT

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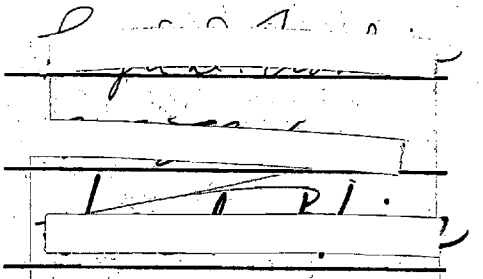

Date Approved by Chairman: June 4, 1956

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STUDIES OF RACEMIZATION RATES IN SOLVENTS OF INTERMEDIATE DIELECTRIC CONSTANT

(117 pages)

Lyman Wallace Morgan

Loyd D. Frashier, Thesis Advisor

ABSTRACT

The effect of the solvent on the rate of racemization of optically active methyl α-bromoesters was studied in nine systems consisting of three different esters in three solvents. Each of the esters, methyl α-bromoisocaproate, dimethyl α-bromosuccinate, and dimethyl α-bromoglutarate was studied in the solvents acetone, acetonitrile, and nitromethane. The racemizations were catalyzed by the ionic bromides tetraethylammoniumbromide or tetrabutylammoniumbromide. In each case the salt concentration was varied over a ten-fold range, from about 0.5 mM to 5 mM in acetone, from about 5 mM to 50 mM in acetonitrile, and from about 10 mM to 100 mM in nitromethane. The ester was studied at two or more concentrations, usually 0.13 M and 0.26 M. The rates of racemization were observed at 25.00° C. and 35.00° C. in a polarimeter using the Hg 5461 Å green line. An accuracy of ±0.5% in the pseudo

first-order rate constant was obtained.

The changes in the pseudo first-order rate constants caused by changes in ester concentration proved to be important and complicated. Methyl α-bromoisocaproate, with only one ester group, had a larger effect on the rate constant than dimethyl α-bromosuccinate or dimethyl α-bromoglutarate, each of which had two ester groups. The increase in ester concentration increased the rate constant in two cases (positive effect), decreased it in nine cases (negative effect), and in seven cases had no effect. By assuming clustering, or non-homogeneous distributions of ester and salt in solution, these effects were explained qualitatively. It was necessary to bring into the discussion the manner of coupling of solvent molecules, and the results were consistent with the generally accepted structure of these solvents; i.e., the rotation of acetone molecules is practically unhindered, that of acetonitrile molecules is hindered by contra-association, and that of nitromethane is hindered by co-association. These concepts were found to be consistent with the effects of these solvents on the second-order rate constants.

The second-order rate constants were obtained using a graphical analysis which also determined the best

ionization constant for the ionic bromide. Tetraethylammoniumbromide was found to have an ionization constant in acetone of 1.5×10^{-2} at 25° C. and 0.8×10^{-2} at 35° C. A few runs of the tetrabutylammoniumbromide indicated 1.7×10^{-2} at 25° C. Two second-order rate constants were assumed in the analysis, one for the bromide ion, and one for the molecule, but the graphically determined rate constant for the molecule was zero. The molecule was apparently too bulky to give a measurable rate. These bromide salts were apparently completely ionized in acetonitrile and nitromethane for concentrations up to 50 mM and 150 mM, respectively, and consequently required no graphical analysis. The butyl salt was used to determine the bromide ion constant for the succinate in acetone at 25° C. to check the value obtained using the ethyl salt. There was no measurable difference between the two values. Because of the effects of ester concentration, the second-order rate constants determined by this graphical analysis were extrapolated to zero ester concentration. A linear extrapolation previously used by Frashier for the same purpose was chosen, and for its use only two ester concentrations were needed. But consideration of the positive ester effect shows that such a linear extrapolation is not correct at high ester concentrations. For that reason, and also since the ester con-

centrations were not determined with high precision, the second-order rate constants lost some accuracy during the extrapolation to zero ester concentration. For this reason, only those seven rate constants which were measured in systems without ester effect are considered accurate to within 1%.

The ethyl salt concentrations are believed to be accurate to within 0.5%. The solvents used were purified to a high degree and dried until phosphorus pentoxide would no longer remove water from them. The bromoesters were synthesized from the corresponding optically active amino acids and purified by batch distillation. The high relative volatility of water made it easy to remove. The esters were hygroscopic, and care was taken to avoid contamination by atmospheric moisture.

The second-order rate constants of the esters increased with the number of ester groups per molecule, and work by de la Mare on similar systems supports this trend. Onsager's "external moment", which is proportional to the permanent dipole moment in simple cases, predicts this trend for ion-dipole reactions where the "dipole" is generalized to include the dipoles other than that of the reaction site.

The effect of the solvent on the reactivity was generally in agreement with expectations. First, the logarithms of the extrapolated second-order rate constants

were approximately inversely proportional to the square of the solvent dielectric constants. The rate did not increase as fast as the correlation predicted as dielectric constant decreased, especially when the data of Todd for methylethylketone were included. This is a commonly observed deviation which indicates that, in polar solvents with dielectric constants below thirty, the local dielectric constant may be considerably different from the conventional value. A second correlation based on Hildebrand's solubility parameter theory was applied. The relative change in the activity of the bromide ion with solvent was assumed to conform to a "regular solution" after the relative sizes of the ion and solvent molecules were taken into account. There is doubt as to the applicability of the equation to polar substances because of the suspected additional entropy effects, but where none is predicted then the equation should apply. The bromide ion is spherical, and it is believed that the effect of its charge can be included in the Van der Waals cohesive energy term. By attributing the major effect of the solvent on reactivity to its effect on the bromide ion, we are assuming that the effects of solvent on the ester molecules and on the activated complex are relatively small and in the same direction. It is suggested that the contra-association of acetonitrile makes it less able

to solvate bromide ions than co-associating nitromethane.

These systems have proven so fruitful that they are believed to justify further study, especially as to the ester concentration effects, with the object of subjecting the data to quantitative correlations and analyses based on molecular properties.

Approved by: Loyd D. Fraenkel

Date: June 4, 1956

CHAPTER I

INTRODUCTION

This investigation was undertaken to study the rates of racemization of three optically active methyl α-bromoesters by ionic bromides in solvents of intermediate dielectric constant to observe some of the effects of the solvent on reaction rate. These racemizations have been shown to proceed by inversion on the carbon-bromine bond by an S_N2 reaction with every substitution followed by inversion for dimethyl α-bromosuccinate (1,2) and for methyl α-bromopropionate (3). It was assumed that dimethyl α-bromoglutarate and methyl α-bromoisocaproate would also racemize, with inversion accompanying every substitution, and that no other reaction was significant under the conditions used. The three esters used are simply called the succinate, the glutarate, and the caproate in what follows.

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(1) Olson, A. R., F. A. Long, Journal of the American Chemical Society, 56, 1294 (1934).

(2) Olson, A. R., F. A. Long, Journal of the American Chemical Society, 58, 393 (1936). (various reaction paths were investigated)

(3) Cowdrey, W. A., E. D. Hughes, T. P. Nevell, C. L. Wilson, Journal of the Chemical Society, (1938) 209. (radio bromine was used)

Three solvents were chosen whose dielectric constants fall in a range intermediate between hydrocarbons and water: namely, acetone, acetonitrile, and nitromethane. This range was considered to offer the best possibility for elucidation of the role of the solvent in reaction rates because the reactivity of ion-dipole reactions in lower dielectric constant solvents will be higher, and measurable reaction rates are possible at salt concentrations so low that the individual ions are from 20 to 100 Å apart. In solvents of lowest dielectric constant this is even more true, but electrolytes are too insoluble in them.

When a solute dissolves in a solvent to produce a non-ideal solution, the excess entropy, enthalpy, and free energy changes, which are measures of the departure from an "ideal" solution, can often be explained in molecular terms such as the volumes, shapes and internal structures of individual molecules and the forces between them. There has been a tendency to employ models of the liquid state with strict limitations on the permissible parameters so that the systems studied could be characterized by a few constants. As often as not, the implications of such models were inconsistent with other results, and it is commonly held that there is no theory of solution which is of general applicability. Thus it is apparently still impossible to predict the direction of a trend unerringly.

For example, experimental interest in the aqueous solutions of the alkali halides stems from the hope that chemical reasoning will explain the order of participation of the members of this readily available family in various processes such as chemical reaction, ion conductance, and viscous flow. With the purpose of learning more about liquid structures, the present study was undertaken from much the same viewpoint. A family of three optically active methyl esters that contained an α-bromine atom were racemized by an ionizable bromide catalyst in a family of three solvents of dielectric constant about midway between that of non-polar solvents and that of water. By making comparisons between these nine systems at 25° and at 35° it was hoped that effects and trends, not observable in aqueous solutions with their large dielectric constants, would be important enough in these chosen solvents to stand out clearly, perhaps for the first time. There was a background of some success, to substantiate such a plan, in the work of Olson and collaborators. In acetone they had observed a relatively large dependence of the second order rate constants on the concentration of the racemate, dimethyl α-bromosuccinate (4). The rate constant decreased

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(4) Olson, A. R., L. D. Frashier, and F. Spieth, The Journal of Physical and Colloid Chemistry, 55, 1860 (1951).

with ester concentration in such a way, that the reciprocal of the rate constant was linearly dependent on the concentration of the ester, to within the experimental error. It is assumed that such dependences in the past have been lumped into an error term such as "salt effect" (5). In keeping with other work on salt effects under Olson's direction, this "ester effect" was interpreted as an adsorption phenomenon. The falling off of the rate constant was attributed to the adsorption of the catalyst, lithium bromide or bromide ion in the racemizations studied under Olson, onto some part of the ester molecule, in such a way as to deplete the solvent of some of its catalyst. Because of the charge on the bromide ion, the site of adsorption was assumed to be on the dipolar ester group. One difficulty arose in this interpretation.

The actual racemization rate had been correlated by assuming it to be the result of two rates, one due to the polar lithium bromide molecule and the other due to its anion, and the correlation made use of a reasonable ionization constant for lithium bromide. Supposing that the adsorption of lithium bromide and bromide ion from the solvent to the ester would be different, two series of runs were made, varying the ester concentration; the first at a gross concentration of lithium bromide of 1.044 mM and the

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(5) de la Mare, P. B. D., Journal of the Chemical Society, (1955), 3180.

second at 20.03 mM. The ratio of the concentration of bromide ion to lithium bromide molecules was 1.70 in the first series and 0.268 in the second. But the ester effects were not measurably different, and this anomaly was looked upon as one requiring the widest possible investigation.

Another explanation had been presented to explain why in the racemization of l-bromosuccinic acid by lithium bromide in acetone the addition of water increases the activation energy. It was concluded (6) that "...on the addition of water a statistical distribution of water molecules between the bromide ions and the acetone molecules, which is largely in favor of the bromide ions, occurs." The adsorption theory as applied to salt effects is similar to the statistical theory as applied to solvent effects and both can formally be considered together as clustering. Experimentally, both should exhibit activation enthalpy effects. Activation entropy effects also would be expected because the number of states which would lead to reaction would be changed by a change in the distribution of molecules. However, the entropy factor as found by these authors, discloses "...a curious and interesting change as the amount of water is increased." (6) As the percentage of water increased from its smallest

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(6) Olson, A. R., and H. H. Voge, Journal of the American Chemical Society, 56, 1690 (1934).

value in dry acetone, the entropy factor first increased, then decreased, and finally attained its highest value in pure water. At the present state of solution theory, quantitative predictions of such bewildering changes with concentration are not expected. For example, changes in rate constants because of concentration changes of a reactant, cannot in advance be estimated even as to direction, let alone extent. It was therefore determined to measure the ester effect in all eighteen systems, nine at each temperature. But, in order to keep the scope of the investigation within bounds, the functional form of the dependence was assumed to be that shown by Olson, Frashier, and Spieth; consequently, in most systems, only two points were taken to establish the ester effect. Since no particular solution model was assumed in this investigation, a statistical approach was used in the selection of components. To compare with Olson, Frashier and Spieth's work, acetone was to be used as one solvent. At least two other solvents would be needed to establish a trend, and for internal comparison it was decided to choose two different solvents with nearly the same dielectric constant. Nitromethane and acetonitrile satisfied this requirement nicely. Thus any effect due primarily to the bulk average dielectric constant D would be about the same in these two solvents, D = 35, but appreciably different in acetone,

D = 20. Similar reasoning led to the choice of reactants: dimethyl α-bromosuccinate, to compare with Frashier's work; dimethyl α-bromoglutarate, similar to the succinate in having two carbomethoxyl groups; and methyl α-bromoisocaproate, different from the other two esters in having only one carbomethoxyl group. If the ester concentration effect were due to the adsorption of the catalyst onto ester groups, then the caproate ought to show an "ester effect" half that of the glutarate and succinate. The choice of bromide was made on the basis of solubility in the three solvents, and the hope of avoiding the complication of parallel reaction paths. Tetraethylammoniumbromide, TeaBr, was chosen, and the large bulk of the molecule was expected to eliminate it as a reactant. An auxiliary matter was the expectation of larger ionization constants for TeaBr than for lithium bromide. A second salt, tetrabutylammoniumbromide, TbaBr, was used to see whether the bromide ion rate calculated for TeaBr would equal that calculated for TbaBr and thus give support to the internal consistency of the data and calculations.

CHAPTER II

EXPERIMENTAL PROCEDURES AND APPARATUS

A. Introduction.--Experimentally, the problem was to prepare anhydrous solutions of optically active α-bromo esters and ionic bromides in polar solvents and to determine the pseudo first order rate constants for the racemization of the esters.

Ionic reaction rates in solvents of intermediate dielectric constant are decreased considerably by traces of moisture, and the main experimental difficulty of this research was the removal and exclusion of water from the materials used. The solvents used: acetone, acetonitrile, and nitromethane; were amenable to drying over phosphorus pentoxide. The salts, tetraethyl- and tetrabutylammonium-bromide, were dried under high vacuum using heat, and esters were sufficiently dried by vacuum distillation. The use of a dry box was avoided by developing procedures for handling these materials on the desk top by which contact with room air was prevented.

The salts and solvents were commercially available, but the esters had to be prepared by brominating optically

active amino acids (7) using diazotization and then esterifying them.

The amount of ester in a reaction mixture was roughly measured by a small syringe, but the salt was carefully pipetted from stock solutions. The stock solution concentrations were made up gravimetrically, and the salt purity was checked by potentiometric titration. This titration was developed until the uncertainty was reduced to a few tenths of a micromole.

The racemizations were followed by polarimetry with a variability which changed from 0.01 to 1/kilominute over the range of rates from 1 to 90/kilominute.

A rough correlation of ester volume and weights gave the following densities:

Succinate (1.46 ± .01) g./ml.

Glutarate (1.42 ± .02) g./ml.

Caproate (1.24 ± .02) g./ml.

A precise value of succinate density was obtained without having protected it from room air.

Succinate (moist) 1.512 g./ml. at 25°

B. The Preparations of Esters

1. Succinate.--To a one liter round bottom flask 35 g. of asparagin and 150 ml. of saturated hydrobromic acid

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(7) Holmberg, B., Berichte, 60, 2194 (1927).

were added and refluxed two hours to hydrolize the amide groups. (When aspartic acid was available, refluxing was omitted.)

The mixture was cooled to 5° after adding to it 93 g. of sodium bromide and 100 ml. of water. Then 35 g. of sodium nitrite was dissolved in 55 ml. of water and added dropwise into the mixture from a separatory funnel slowly enough to take an hour. To keep the temperature below 5°, the one liter beaker was kept in ice and water, and 200 g. of chipped ice was added as required. An electric stirrer kept the mixture agitated. The evolution of bromine vapors required the use of a hood. Ten minutes after the last nitrite had been added, a cool mixture of 15 ml. of concentrated sulfuric acid and 75 ml. of water was added. Ten minutes thereafter the bromoacid was extracted with ether using a five liter separatory funnel. One portion of 200 ml. and three portions of 100 ml. each were used. Each extraction mixture was shaken for ten minutes. Each extract was transferred to a seven inch diameter, deep evaporating dish. The dish was warmed under a hood by a hot plate turned low, and a blower was directed on the contents. The acid crystallizes without difficulty, but it forms a crust over the water which accumulates from the wet ether. As soon as most of the ether had evaporated, the hot plate was turned off, and the crust was scraped

to one side. The acid dries to pale yellow crystals.

To recrystallize the acid, 125 ml. of acetone was used to dissolve it, and the solution was filtered through a fine sintered glass filter. After adding 150 ml. of thiophene-free benzene, the mixture was blown down to one-tenth volume. The product was recovered by filtration, and washed with 100 ml. of benzene yielding about 25 g. of snow white needles.

The acid was refluxed for two hours with 300 ml. of methanol containing 3.6 ml. of concentrated sulfuric acid. After adding 480 ml. of water, the ester was extracted with ether. One 300 ml. portion and three 100 ml. portions were used and the extract was evaporated overnight. The water phase was removed with an eye dropper. The ester was heated to 60° for two hours and pushed through a fine sintered glass filter with cylinder nitrogen. The ester was put into a special vacuum still with a fine capillary whose tip touched the bottom of the charge. Water and methanol were removed at room temperature by applying a vacuum measuring about ten microns of mercury. After the vigorous bubbling subsided, the charge was distilled over at from thirty to fifty microns and at 53° to 56°. About 14 ml. of final product can be increased to 18 - 19 ml. by obtaining a second crop of the acid from the acid benzene filtrate. The ester was stored in small portions, and just prior to

use, or after several exposures to the air, the portion to be used was redistilled to dry it. One of the chief variabilities of this work lay in not having realized early the tendency of the anhydrous ester to pick up water from the air.

2. Glutarate.--The glutarate preparation was modeled after that of the succinate with the following modifications:

As starting material, 35 g. of glutamic acid was used, and the hydrolysis step was omitted. The bromoglutaric acid could not be crystallized at a convenient temperature (a low temperature crystallization using acetone and dry ice would have been useful), nor could the oil be distilled at 100 microns. Any attempt to increase its vapor pressure by warming led to the evolution of bromine and the change of the oil to a glassy substance. A molecular still was not available. As a consequence, the crude acid was esterified. The ester distilled at about 60° and at 20-30 microns yielding about 18 g.

3. Caproate.--The caproate preparation was modeled after that of the succinate with the following modifications:

As a starting material 35 g. of leucine was used, and the hydrolysis step was omitted. Since the acid resisted freezing, it was purified by vacuum distillation using the ester still. The acid boiled over at about 90° under an absolute pressure of about 200 microns. A light

yellow oil was recovered weighing 38 g. The acid was esterified using the succinate procedure, and the ester was fractionally distilled below 35° at 0.5 mm. Since the acid and its ester were of comparable volatility, a residue of one milliliter was retained, and the ester was titrated for acid using phenol red as an indicator. The ester was sufficiently less volatile to contain less than one-half per cent by weight of the acid, but the undistilled residue contained about twenty-five per cent by weight of acid.

C. Purification and Drying of Solvents and Salts

1. Purification of Acetone.--Three liters of C.P. acetone was treated with potassium hydroxide pellets and crystals of potassium permanganate for twenty-four hours and poured off. Permanganate was added (8) until the color persisted for a few hours and then more pellets were added to remove the acidic products of oxidation. The acetone was decanted and distilled through a four foot column one inch in diameter carefully packed with one-eighth inch single-turn glass helices. The column was insulated with a silvered vacuum bellows jacket. The reflux ratio was about three and the product takeoff was about two drops per second. Only twenty or thirty milliliters of forecut was discarded, and the overhead temperature remained constant ± 0.05° until

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(8) Bramley, A., Journal of the Chemical Society, (1916), 109.

there was only twenty or thirty milliliters of residue. The forecut was not identified, but the residue had the odor of acetone polymer. The distillate was dried over freshly dried drierite, and enough water was removed to warm the entrance section of a one and five-eighths diameter column of absorbent. This acetone may have been dry enough for reproducible kinetics, because on subsequent treatment of its vapor by phosphorus pentoxide, there were no observable phosphoric acid droplets formed. However, there was no attempt to make such use of it. Instead, the recovered dry acetone was stored in a two liter pyrex bottle as a stock solution. For reaction rate runs, portions of about two hundred and fifty milliliters were vaporized over phosphorus pentoxide (9) and scrupulously kept from contact with room air.

2. Purification of Acetonitrile.--One kilogram of Matheson acetonitrile was treated with potassium hydroxide pellets for two days (10). The solvent was then decanted into a flask containing calcium chloride to remove ammonia by the formation of an addition compound. After standing for a week over the chloride with swirling each day, the acetonitrile was decanted into a flask and phosphorus pentoxide

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(9) Timmermans, J. and L. Gillo, Roczniki Chemi, 18, 812 (1938).

(10) Cowley, E. J. and J. R. Partington, Journal of the Chemical Society (London) (1933), 1252; (1935), 604; (1936), 1184.

was added. Within three hours yellow gelatinous granules formed. The solvent was decanted and another batch of pentoxide was added. This time the pentoxide remained powdery, but the solvent became white. Distillation yielded a small forecut and about one liter of distillate boiling at 81°, which had an acidic odor like hydrogen cyanide. This material was stored until needed. For final purification it was repeatedly treated with phosphorus pentoxide, distilling from it under vacuum each time. As a test, after having stood twelve hours over the pentoxide, the solvent was required to remain colorless and the desiccant, a white powder, visibly unchanged; otherwise it was treated again. The final distillate did not have the characteristic odor usually associated with acetonitrile, but had a sweetish odor which could not be distinguished from that of very pure nitromethane.

During distillation the solvent formed a gel with the pentoxide but distilled from it without difficulty. The principal difficulty was bumping, but by separating the boiler from the receiver by two adaptors and a Claisen distillation head, the surges of entrained liquid were successfully kept from the receiver. The receiver was kept below -30° and the back-pressure on it below 1 mm. Hg. absolute.

3. Purification of Nitromethane.--Fifteen hundred grams of Commercial Solvent nitromethane was fractionally distilled at about 100 mm. pressure through the same column used for acetone. Vacuum fractionation was thought to be necessary because decomposition apparently took place slowly at the normal boiling point. An Emil Griever pressurestat held the vacuum to within one millimeter as long as the column head did not leak. This requirement was met by choosing a Newman (11) type take off stopcock, which has a drip tip and a lubricant well the solvent cannot attack. Nitromethane does not flow freely through one millimeter tubing since it does not wet glass very well; therefore, a two millimeter bore is better. The boiler was a two liter, three necked flask. The center neck bore a thermometer, and the boiler temperature was held to 60°.

The distillate was shaken with one per cent silver nitrate to remove cyanides. Using methanol and ice as a coolant, most of the water was removed on a fritted glass filter as snow white crystals from the solvent. Since the solvent gave positive indications for aldehyde by the Fuchsin and Benedict tests, crystals of potassium permanganate were added until the purple color persisted for three hours. A small portion of the solvent was distilled

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(11) Carney, T. P., "Laboratory Fractional Distillation", MacMillan Company, New York, 1949, p. 108.

and shown to have a negative Fuchsin test; i.e., the water layer remained colorless while the nitromethane layer became faintly pink after a few hours. From this point on the solvent was repeatedly treated with phosphorus pentoxide powder (12) and batch distilled from it under vacuum until phosphorus pentoxide remained white and powdery for twelve hours in the water white solvent. The set-up was the same as that used for acetonitrile. Bubbles came from the cold boiler charge before distillation commenced. These had previously been identified as (13) carbon monoxide and were pulled on through the system before the receiver was cooled to begin distillate recovery.

It might have been better to have fractionated the solvent after treatment with silver nitrate, potassium permanganate and the removal of water. With the principal impurities removed, the fractionation would have done a better job of purifying.

4. Note on Purification by Fractional Freezing.--It was found that the purity of distillate nitromethane could be followed very well by its freezing point. For extended work with this solvent it would seem desirable to arrange for the final purification to be fractional freezing.

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(12) Wright, C. P., D. M. Murray-Rust, and H. Hartley, Journal of the Chemical Society, (1931), 199.

(13) Gardner, J. H., Ph. D. Thesis, Harvard University, 1950.

Fractionally freezing each portion just prior to use, the purity could be measured by the melting point of the crystals right in the stock solution flask by a sealed-in thermocouple or resistance thermometer. This would give an accurate, quantitative evaluation of the purity of each solvent preparation and do much to improve the reliability of solvent studies. It is anticipated that acetonitrile would submit easily to the same treatment.

Attempts to use fractional freezing to purify the succinate ester were unsuccessful because of an unexplained cooling curve. The less symmetric glutarate and caproate were even less amenable to freezing; they formed glasses in which no nuclei ever were coaxed to form, even after hours of cooling and warming.

5. Purification of Tetraethylammoniumbromide.--Eastman white label TeaBr was purified by recrystallization from ethanol.

One liter of C.P. ethanol was distilled from magnesium amalgam to dry it for use as a solvent for TeaBr. About 100 g. of TeaBr was charged to a 500 ml. flask fitted with a Claisen distillation head topped with a dropping funnel. The apparatus was protected by a tube packed with fresh drierite. Ethanol was added in small portions with gentle refluxing after each addition, the Claisen head acting as an air condenser. To dissolve

all the salt, about 140 ml. of ethanol was required. The hot solution was poured through the air onto a small suction filter provided with a 500 ml. round bottom flask receiver. Water aspirator suction was used with a water trap and a drying tube. The hot filtered solution was stoppered and cooled, then immersed in a methanol-dry ice mixture with constant shaking. Agitation kept the crystals small and free of the flask so they could be poured easily onto a seven inch diameter fritted glass filter. Suction was used to pull most of the mother liquor through, then a large stopper containing a dry nitrogen connection was placed in the filter top. Dry nitrogen was used to push out the balance of the mother liquor; then dry nitrogen was passed through the bed for twenty minutes to dry the crystals. A spatula was used to scrape the salt into weighing bottles, care being taken to grind all lumps and obtain a free flowing powder. The yield was seventy-five per cent. On drying in a high vacuum (estimated 1 mμ. Hg.) for ten hours at a temperature of 115°, only about 0.1% weight loss was measured. It remained white and free running stored over calcium chloride for a year. Exposed to the air, the salt picked up moisture slowly. As a precaution, the salt was baked under high vacuum just before use.

6. Purification of Tetrabutylammoniumbromide.--TbaBr was

kindly provided in a sufficiently pure state by E. P. Blanchard. Its preparation and purification are given in his thesis (14).

7. Drying of Acetone with Phosphorus Pentoxide.--A procedure for preparing about 300 ml. of pure anhydrous acetone was developed which dried the acetone by passing its vapors over phosphorus pentoxide. By keeping the pressure reduced, no acetone would condense on the apparatus at the temperature of the room. Acetone containing less than 0.001 wt.% H_2O was prepared by Timmermans and Gillo (9) in this way.

The phosphorus pentoxide was dusted onto 1/2 inch lengths of 7 mm. glass tubing. Moisture in acetone promotes its polymerization on phosphorus pentoxide, and reddish brown drops of liquid form which drip from the packing. Because of the dripping and the need to assure good distribution of packing across the cross section of the column, the column was arranged vertically. Acetone which passed up through at least 6 inches of unmoistened packing was considered dry. Such unmoistened packing was turned from snow white to a buff color usually, but the dryness of its appearance was not altered. Bumping was troublesome because of the phosphorus pentoxide powder which was sometimes blown over into the receiver. This

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(14) Blanchard, E. P., M. S. Thesis, Georgia Institute of Technology, 1955.

inevitably led to polymerization and such solvent was re-vaporized over fresh packing. A clear liquid without color always resulted if bumping was controlled. Bumping was prevented by removing a stopper from a fine capillary tube to allow room air to bubble through the vaporizer. Excessive accumulation of air in the apparatus was easily detected by a vacuum manometer and easily removed by pumping.

The air dried apparatus was first assembled except for the boiler and drying column. Lubriseal was used on all ground glass connections, and, except for the vapor path, gum rubber vacuum tubing was used for connections. Dry C.P. phosphorus pentoxide was poured over about 500 cc. of short pieces of 7 mm. glass tubing in a quart bottle--enough to coat the glass packing without excess powder. Air dried packing was used because oven dried packing would not hold the powder on its surface. Gentle tumbling was used to spread the powder over the packing. Glass wool was pushed down through the column to support the packing above the vapor inlet. A paper funnel fashioned from an 8 x 11 inch sheet was used to guide the treated packing below the ground surface of the 45/50 joint at the column top. By rotating the column while pouring the packing down through the paper funnel, the packing was spread uniformly across the column. Additional glass

wool was pushed onto the top of the packing to hold back phosphorus pentoxide should bumping occur.

The drying column was placed on the system with a No. 24 glass stopper in the vapor inlet, and the system was checked for leaks. It was considered tight only if a full vacuum (0-1 mm. Hg.) held for 5 minutes. Disconnecting the vacuum pump after closing the pinch clamp, air was permitted to fill the system slowly (2-3 mm. Hg. pressure increase per second). Attempts to fill from the bottom of the column often resulted in phosphorus pentoxide powder being deposited in the receiver and consequent polymerization of the product. The boiler containing ca. 350 ml. of purified, partly dried acetone was placed on the system at the vapor inlet of the drying column and cooled in a dry ice-acetone bath to lower the acetone vapor pressure in the boiler. The vacuum pump was next applied cautiously by controlling the pinch clamp until the pressure was reduced to 10 or 15 mm. in order to protect the pump, and the final cold trap was cooled before the pressure dropped below 100 mm. During the pumping, air, previously stored in the $\overline{\$}$ 10/30 bubbler chamber, bubbled through the cold acetone. If it did not, the capillary was too small; if the bubbles were large (1-2 mm. diameter) the capillary was too large.

With a cold trap cooled to -80° on one side and

dry phosphorus pentoxide on the other, and with the pressure down to 10 mm. (to improve diffusion), the receiver and connection tube were deemed dry. Flaming was found to be unnecessary. The coolant was next removed from the boiler and a glass-col heating mantle was placed there and connected to 50 volts. Dry ice and acetone were added to a Dewar flask which was placed around the receiver to begin the collection of product. Control over the vacuum was effected by letting air be pumped out through the pinch clamp or be admitted through the $\overline{\$}$ 10/30 joint of the bubbler. This last procedure always initiated boiling when the boiler liquid threatened to bump. Air admitted this slowly never blew over any phosphorus pentoxide powder. The back pressure on the receiver was held to 5-10 mm. throughout the distillation.

The distillation was stopped when the residue fell to 20-30 ml. because it was observed that the last portion wet a disproportionately large part of the packing and therefore probably retained most of the initial moisture in the acetone as charged to the boiler. By admitting air slowly (3-5 mm. pressure increase per second) and warming the receiver with water heated to 40-50°, the receiver contents were brought to room temperature and pressure. The receiving flask was slipped from its connecting tube and stoppered with a weighing-bottle stopper which was

greased with Lubriseal and secured by a rubber band.

If the acetone had been sufficiently dried previously, (over efficient Drierite, for example) most of the phosphorus pentoxide would have turned a buff color. The column was removed from the system as soon as the distillate was safely stored and emptied of its packing. The packing was usually shaken out into a 400 ml. beaker of water in which the phosphorus pentoxide and its acetone polymers dissolved; the dissolution occurred rapidly with spattering. If, on the other hand, the acetone was moist enough to leave the bottom packing covered with red tar, the dissolution required about an hour.

8. Drying of Acetone with Drierite.--A procedure for preparing about 2 l. of pure, relatively dry acetone was used which dried the acetone by passing its vapors over Drierite freshly dehydrated in the same apparatus used to dry it with phosphorus pentoxide.

Drierite heated to 235° in an ordinary oven will revert to a "soluble anhydrite" form which maintains its high-drying efficiency until converted to the hemihydrate containing 6.6 per cent water on a dry basis (15). The reaction takes place much more rapidly and completely if the Drierite comes in contact with the vapors of the solvent being dried because diffusion of water molecules into

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(15) Hammond, W. A., and J. R. Withrow, Industrial and Engineering Chemistry, 25, 1112.

the pores of the Drierite particles is so impeded by liquid solvent. The liberation of heat, ca. 300 cal. per gram of water absorbed, allows the progress of a hot zone up the column to be followed. Thus the distillation can be stopped before the capacity of the Drierite has been spent. The acetone so dried has the exact density of pure acetone over the range 0-35° to four decimal places (16). No attempt was made to use acetone dried over Drierite for a reaction rate study.

D. Preparation of Salt Stock Solutions.--The required weight of salt was spooned into a 10 ml. volumetric flask and dried at 115° for ten hours under a vacuum of about 1 mμ. Hg. The salt was held in an atmosphere of dry nitrogen until needed. The volumetric flask was stoppered with a dry stopper as soon as it was removed from its sealed container. It was weighed. A 100 ml. volumetric flask, well ground by its own stopper and 600 mesh carborundum, was provided with a glass chimney having a dry nitrogen inlet to sweep the room atmosphere away from the top of the volumetric flask. The glass stopper was removed from the volumetric flask and lubricated. A glass tube connected to dry nitrogen was placed down through the neck

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(16) Timmermans, J., Physics-Chemical Constants of Pure Organic Compounds, Elsevier Publishing Co., New York, 1950, p. 355.

of the flask to sweep out all the air it contained. A specially made funnel just having been heated to 100° so salt would not adhere to its surface, was slipped inside the chimney and into the mouth of the flask. Its large end was just large anough to receive the neck of the 10 ml. volumetric containing salt. The large volumetric, chimney, and funnel were held horizontally, the top of the small volumetric was removed, and it was inserted into the funnel. In this way the salt could be transferred without exposure to the air. A quick shaking motion sufficed to get all the salt into the large volumetric. The small volumetric was removed and stoppered so it would not pick up water. A cork stopper was inserted into the large volumetric. The 250 ml. Erlenmeyer flask was provided with a dry nitrogen chimney and then its stopper (lubricated) removed. A 100 ml. pipet, supported by gum rubber vacuum tubing from a strand and attached to a small vacuum pump, was used to withdraw somewhat more than 100 ml. of solvent. By turning a three-way stopcock, a small amount of dry air was admitted to the pipet to prevent air bubbles from dribbling up. The stopper for the Erlenmeyer flask was wiped, relubricated, and put back on while dry nitrogen continued to sweep up the chimney. Then the cork stopper was removed from the 100 ml. volumetric and solvent was added from the pipet by once again admitting dry air to

its top through the three-way stopcock. Sweeping dry nitrogen up the chimney during this delivery kept room air from contacting the solvent. For nitromethane and acetonitrile simple swirling after half the solvent had been added dissolved the salt. For acetone, three glass beads were added for subsequent shaking because of the slight solubility of TeaBr in acetone. Solvent was added until the solution came up to the mark. The lubricated stopcock was placed on the volumetric and a rubber band was used to make certain the stopper did not get pushed loose in the mouth by vapor pressure increase of the stock solution. About six or eight hours in a mechanical shaker was needed to dissolve the salt for a 6 mM solution of TeaBr in acetone. The butyl salt was quite soluble in acetone. For solutions more concentrated than those used in this work, some other procedure was indicated because large quantities of salt (2.5-3.0 g.) tended to hang up in the small funnel during transfer. It is suggested that a provision for heating the salt under vacuum while in the 100 ml. volumetric would be sufficient.

E. Experimental Procedures and Calculations for Bromide Ion Rate Constants.--A Bellingham and Stanley model A polarimeter was used to make the optical readings. A Wratten number 61 filter was used with a mercury lamp to provide 5461 A light. A constant temperature bath

had been built previously to accommodate polarimeter tubes three decimeters in length (17). Notches had been cut to position the tube in the light path. A rack holding five other tubes in the same water bath was used during long runs. The temperature varied in the bath as the heater was turned on or off by a few thousandths of a degree. This temperature variation was smoothed in the tubes by the time lag of the tubes so that refractive index "shadows" never appeared after the tubes once came to temperature. There was also a few thousandths of a degree difference from top to bottom in the bath due to the loss of heat from the surface. Both variations could have been reduced by insulating the top of the bath.

Polarimeter readings with acetone in the tube were taken first until they checked to within 0.02°. The reaction solution was then made up and placed in the water bath. By sensitizing the eye first, the early readings were improved.

Reaction mixtures were made up in 25 ml. volumetric flasks. Attention was paid to the thermal expansion of acetone, because the molarity of the salt stock solution was appreciably affected sometimes by room temperature changes. A polarimeter tube previously filled with dry nitrogen was filled as quickly as possible from the small

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(17) Todd, J., M. S. Thesis, Georgia Institute of Technology, 1951.

flask. The solution contacted only dry nitrogen while flowing from the flask into the tube except for several seconds while the emptied flask was set down and the top cap of the polarimeter was screwed on.

The angle in degrees, θ, and time in minutes, t, were recorded as read. Subtracting the zero reading, θ_o, from the angle gave the optical rotation, α. Its natural logarithm was plotted as a function of time on graph paper to arrive at the best straight line for each run. Runs were given a letter and a number. The letter designated the solvent (S for acetone, A for acetonitrile, and N for nitromethane) and the number designated the number of the run in that solvent. Because of the poor accuracy, Run N6 was repeated under better control and the rate was determined to be $10.3/10^3$ min. showing the error to have been about 10%. The data of Run N6 was then examined with a "Student's t" confidence limit test to see if the inaccuracy of such poor appearing data could be shown statistically. The slope, based on a least squares calculation, was determined to within 5% at a 50% confidence level, to within 17% at a 95% level. The calculated rate was $11.8/10^3$ min. and that determined "by eye" was $11.3/10^3$ min. One difficulty attending such an evaluation of this run data arose because the ordinarily published statistical tables consider that the numbers as used have random

scatter and this does not apply here. The random error lay in the optical rotation, and not in its logarithm as assumed; the logarithm expands the scatter of small numbers. By weighing those points most heavily that occurred at large optical rotation, a better line results. This accounts for the improvement over the least squares slope of Run N6 shown by the slope arrived at by inspection. In summary, it was found that a precision of ±0.5% was attainable, and judging the best slope by eye was sufficient to establish that degree of precision.

The slope was halved to obtain the pseudo first-order rate constant since the inversion of one molecule reduces the optical activity as much as destroying the activity of two; $k = \Delta \ln \alpha / 2(\Delta t)$ min. For those solvents in which the salt was apparently strong, the second-order rate constant was obtained by passing the best straight line through plots of k versus salt concentration, c(M), and dividing by c. Tetraethylammoniumbromide was apparently strong in acetonitrile and in nitromethane to permit this. Because of the dependence of the pseudo first-order rate constant on the ester concentration, graphical plots of k versus c were all made at the same ester concentration, 0.13 M. It was felt that extrapolated values of k at zero ester concentration, k_o, involved so much uncertainty that it would be better to make graphical comparisons at actually

measured rates. Rates for the succinate in acetone at 0.13 M had to be extrapolated from 0.26 M, but the ester concentration effect was better determined in this case.

Figures 1, 2, and 3 show plots of k versus c for acetone, acetonitrile and nitromethane respectively. For acetone, there was a pronounced curvature in k versus c indicating that the salt was weak. By assuming an ionization constant K and a separate reaction path for the undissociated molecule, k was set equal to

$$k_1[\tfrac{K}{2}(\sqrt{1 + 4c/K} - 1)] + k_2[c - \tfrac{K}{2}(\sqrt{1 + 4c/K} + 1)]$$

where k_1 is the bromide ion rate constant and k_2 is the salt molecule rate constant. A graphical procedure was derived by which to solve for k_1, k_2, and K; the procedure is derived in Appendix I. The correlation gave zero as the best value for k_2. The values of K found in acetone for the succinate was assumed to hold for acetone containing glutarate and caproate as well. All of the good runs made during this work are placed on these three figures. There was no way to look for a k_2 in acetonitrile or nitromethane because K was so large.

In order to present all of the ester concentration effects on one figure, after 1/k had been plotted as a function of ester molarity, M, its zero ester concentration intercept, k_o, was used to plot k_o/k versus M in Figure 4.

This sufficed to show how the ester concentration effects relative to k_o varied from ester to ester and from solvent to solvent. However, it should be noted that these slopes are not the same as those used by Olson, et al. (4). In other words, the slopes of the lines in Figure 4 are not equal to "b" in $1/k = 1/k_o + bM$ but instead are equal to "a" in $k_o/k = 1 + aM$ where $a = bk_o$.

CHAPTER III

RESULTS

A. Experimental Results.--Pseudo-first order reaction rate constants were obtained for the racemizations of the succinate, glutarate, and caproate esters by TeaBr in acetone, acetonitrile, and nitromethane at 35° and at 25°, and at different ester concentrations. These pseudo-first order rate constants are presented in Figures 1, 2, and 3. All of the experimentally determined rate constants appear on these three figures. The change of rate constants as functions of the concentration of the ester are presented in Figure 4. The calculated second order bromide ion rate constants are shown in Figure 5 as functions of temperature.

Graphical plots of pseudo-first order rate constants versus TeaBr concentration in acetone have a slight curvature. This was interpreted to mean that TeaBr is a weak salt in acetone. Sufficient points were measured for the succinate to give the ionization constants 15×10^{-3} at 25° and 8×10^{-3} at 35°. For the glutarate and caproate these ionization constants were assumed to apply. These plots in acetonitrile and in nitromethane were straight lines to within the experimental accuracy up to the highest concentrations of TeaBr used.

The caproate reacted more slowly than the succinate and glutarate in all three solvents. The glutarate appears to be somewhat slower than the succinate in all three solvents, as shown in Figures 1, 2, and 3. But the plots are for a concentration of 0.13 M for each ester: and Figure 4 shows that the ester concentration effects of the glutarate and succinate are such as to cause the second order bromide ion rate constants for the succinate and glutarate to reverse between 35° and 25° in acetone. Figure 5 shows the reversal.

The essential data of all runs appear in Tables 1 through 6 in Appendix III: i.e., the salt concentrations, the ester concentrations, and the graphically determined pseudo-first order rate constants. For those runs which were used for ester effect calculations, the reciprocal pseudo-first order rate constants are given.

The effects of ester concentration on rate are given in Table 7, the calculated second order bromide ion rate constants are given in Table 8, and the calculated enthalpies and entropies of activation are given in Tables 9 and 10 respectively.

The graphical determinations of K for TeaBr in acetone at 25° and at 35° are shown to be 1.5 10^{-2} and 0.7 10^{-2} 1./mole respectively, in Figures 6 and 7. Also, K for TbaBr is shown to be 1.7 10^{-2} 1./mole.

B. Comparison of Results.--The second order bromide ion rate constants have been compared in two ways. First, consider the direct effect of the solvent on rate. There are three esters and two temperatures giving six combinations which were used in each of three solvents. Choosing the rate constant in acetonitrile as the standard and the taking of ratio as the basis of comparison, the relative rate constant of each combination in acetone was found to be 25.5 ± 3.5. The relative rate constant in nitromethane was 0.54 ± 0.07. Second, consider the effect of ester structure. Once more there were six combinations, this time owing to three solvents and two temperatures. Choosing the rate constant of the glutarate as the standard, the relative rate constants for the succinate and caproate were 1.28 ± 0.18 and 0.186 ± 0.025 respectively. The errors indicated are arithmetic averages.

The effects of ester concentration on rate as shown in Figure 4 were so interesting that they were searched for indications of trends. The slopes of the lines drawn through points of k_o/k versus ester molarity were taken to be measures of the effect of ester concentration on rate. First, temperature was considered. In acetone the increase of temperature from 25° to 35° caused the effect to increase: but in acetonitrile and nitromethane the increase in temperature caused the effect to disappear.

Second, ester structure was considered. The caproate showed the largest effects, both positive and negative, while the succinate and glutarate effects were more or less similar: the scatter of these latter was surprising in view of the similarity of their structure.

The direct effects of temperature on rate were compared in the customary calculated values of enthalpies and entropies of activation. The lack of regularity was disappointing. Comparison of the enthalpy of activation of the succinate in acetone calculated here, 18.9 kilo cal./mole, with that calculated by Frashier (4) 15.66 kilo cal./mole, is even more disappointing. The Beckmann differential thermometer used could hardly have been so inaccurately set as to have been responsible for so large an error. The scale was proven linear $\pm$ 0.01° using a platinum resistance thermometer calibrated by the Bureau of Standards. Sodium sulfate which had been recrystallized three times was used to set 32.384°. The 25° setting was obtained using a separate Beckmann compared for linearity with the first, and a 10° differential temperature was obtained from a long stem thermometer having 0.02° graduations calibrated at the ice point, the steam point, and the sodium sulfate point. Besides, there is no indicated systematic error between the two calculations: Frashier's rate constant at 24.9° is higher than that calculated here, while his

constant at 35° is lower. Knowing that water was a serious poison for these rate studies from the onset of this work, it is not unlikely that the solutions used were somewhat drier than Frashier's. This would help explain the difference at 35°, especially since Runs S54, S55, and S56 indicated that water is roughly three times as effective in lowering rates of succinate in acetone at 35° as it is at 25°: i.e., if $1/k = 1/k_o + (c/k_o)(H_2O)$, c obtained here at 35° = 3.66 whereas Frashier (4) reported c = 1.39 at 24.9°C. At the lower temperature, if there were more water in Frashier's solutions, the rate would have been somewhat lower than that reported here. In other words, we might conjecture that at 25° there was more water in the solutions used in this work while at 35° there was more water in Frashier's. However, the runs of succinate in acetone at 25° were not made until the very last of this work, after the sensitivity of esters for water was discovered. That means that the solutions used at 25°, if any different in water content at all, were drier than those used at 35°. This suggests that we discard the water contamination hypothesis.

Consideration of the ionization of lithium bromide as compared to TeaBr may offer a more plausible explanation. Frashier used an average value for the ionization constant of lithium bromide $K = 3.3\ 10^{-4}$ at 25° and at 35°. In this

work K has been solved for at each temperature and found to be 15 x 10^{-3} at 25° and 8 x 10^{-3} at 35°, indicating a negative enthalpy of ionization. If the lithium salt also had a negative enthalpy of ionization it would follow that the use of an average K could indicate fewer bromide ions at 25° and more at 35° than were actually present. This in turn would cause the calculated second order rate constants to be larger at 25° and smaller at 35° than were calculated by Frashier, the very discrepancy we set out to explain. If, then, the enthalpy of ionization of lithium bromide in acetone is negative, the type of discrepancy between Frashier's data and the data obtained here might be explained.

CHAPTER IV

DISCUSSION OF RESULTS

A. Introduction.--The second-order reaction rate constant for the racemization of α-bromo aliphatic methyl esters by two tetraalkylammoniumbromides in solvents of intermediate dielectric constant has been varied not only by changing the solvent, the temperature, and the structure of the ester, but also by changing the concentration of the ester. So far as is known, changing the bromide salt and its concentration has not affected the rate constant, but the ionization constants of the salts necessary to correlate these data were high. In acetone they were about five times that indicated by conductance experiments, 16×10^{-3}(m/l.) as compared to 3.29×10^{-3} (18); in acetonitrile and in nitromethane they appeared strong at the concentrations used. A parallel reaction path due to the undissociated bromide molecule was assumed (4), but it appeared to be negligible. Thus there has appeared no evidence of a "salt effect" except insofar as the ester has assumed the role of a "salt", and that the ionization constant of the salt seems high. An ester effect was expected, as was

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(18) Reynolds, M. B. and C. A. Kraus, Journal of the American Chemical Society, 70, 1709 (1948).

pointed out in the Introduction, but the observed variation of it with molecular structure, temperature, and solvent, and the extent of its influence, were totally unexpected. Consequently, the trends of the effects of ester concentration were not followed in detail.

B. The ester concentration effect.--The addition of ester into a solution of solvent and salt affected the second order rate constant in most of the systems studied. In nine of the systems the rate constant was decreased, in seven it did not change, and in two it was increased. Previous work on these effects (4) was interpreted in terms of an adsorption of salt anions and molecules onto ester molecules, the particles so adsorbed being assumed unavailable for reaction with other ester molecules.

The effects of ester concentration were firmly established and, in some degree, bracketed, but the effects of ester concentration on the rate constant are difficult to explain with the data at hand. Even the effects of the solvent, the temperature, and the structure of the ester on the rate constant were confused by the ester concentration effect. It had been thought that extrapolation of all rate constants to zero ester concentration would rid them of ester concentration variability, and for that purpose an equation derived by Frashier was employed. Its success, as used by him for dimethyl α-bromosuccinate in acetone at

25°, did not prove its applicability in general. But since it followed closely the functional dependence of Olson's adsorption-type salt effect equation which had been remarkably successful in correlating salt effect data with high precision (19), it was considered reliable. Applying it to this work and noting in particular the effect of the caproate concentration in acetonitrile at 35°, we realize that Frashier's equation cannot apply unless modified because it does not explain an increase in rate constant with increasing ester concentration. These authors did suggest an alternate interpretation. In their words, "Although we are here ascribing the effect to an association of the bromide with the ester groups, the possibility that the main effect is due to an association between an ester group of one molecule with a carbon-bromine dipole of another ester molecule should not be overlooked." (4)

It can be seen from Figure 4 that the extrapolated value of the rate constants at zero ester concentration could be changed a great deal by using a different formula. Consequently, the relative rate constants discussed further on are not well established, and the effects of solvent, temperature, and ester structure are not precisely determined. This is especially true for the positive ester

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(19) Olson, A. R., and T. R. Simonson, Journal of Chemical Physics, 17, 1196 (1949).

concentration effects in acetonitrile since the plots as drawn indicate an infinite rate constant at a finite ester concentration; i.e., the plots cannot actually be straight lines, as drawn, but must be curved. This acetonitrile system appears to be the one most likely to yield valuable ester effect data in subsequent work.

Although only four points are involved in the positive caproate and glutarate concentration effect, there is no good reason for discarding them, and this can be shown by the following critique. The possibility of the esters having been impure was to be considered first because they were new compounds. The α-bromoisocaproic acid which was esterified had been fractionally distilled under vacuum. The ester derivative was also fractionally distilled, and checked by titration at 0° for acid; the acid was found to be 1/2 wt.% or less. Thus the purity of the caproate seems to have been satisfactorily proven. The α-bromoglutaric acid could not be fractionally distilled, but its ester offered no difficulty to such treatment. The same stock solutions of TeaBr and acetonitrile were used in all four runs, and the reproducibility of the pseudo-first order rate constants in acetonitrile was ± 0.01 x 10^{-3}/min. At 25°, where no ester concentration effects were observed, the agreements between pairs of runs were:

Runs A16 and A17, $k_{xpt.}$ = 8.48 and 8.49 for succinate

Runs A20 and A21, $k_{xpt.}$ = 6.36 and 6.36 for glutarate

Runs A18 and A19, $k_{xpt.}$ = 1.27 and 1.27 for caproate

That the following particular four runs should be in error seems unreasonable. In Runs A22 and A23, $k_{xpt.}$ = 25.1 and 26.3, for glutarate; in Runs A24 and A25, $k_{xpt.}$ = 4.82 and 5.15, for caproate. Being caught off guard by the importance and variability of the ester concentration effects, then, the data obtained do not permit a clear interpretation of them, but the existence of these effects both negative (decreasing the rate constant) and positive (increasing the rate constant) appear experimentally verified.

The following plan will be adopted in an effort to discuss the results of this research as fully as possible. The variability of the rate constant due to all of the other effects will be noted using extrapolated, zero ester concentration values, and then the ester effects will be examined for possible trends so as to derive an idea of their origins and implications. Finally, some theorems applicable to solvent effects in general will be stated which seem to be borne out by the experimental results of this work.

C. The direct solvent effect.--The rates of racemization varied so regularly from solvent to solvent, that there is no difficulty in getting a trend in the direct effect of

the solvent on the rate constant. Taking the rate constant of each ester in acetonitrile at 25° and then at 35° as a basis, the relative rate constants in the three solvents were: 25.5 ± 3.5 : 1.00 : 0.538 ± 0.071 in the order acetone : acetonitrile : nitromethane; or roughly speaking, 25 : 1 : 0.5.

Following the treatment of ion-dipole reactants given by Amis (20), we would expect the logarithms of the rate constants to vary inversely with the square of the dielectric constant. When all of the eighteen constants obtained in this work are plotted in this way, the maximum and minimum slopes which can be drawn through data points are within 10% of the slope of the best average line. As a check for this plot, the values obtained by Todd (17) for the bromide ion rates at 25° and 35° in anhydrous methyl ethyl ketone for the succinate were added in with the data obtained in this work. Using 18.9 as the dielectric constant of methyl ethyl ketone (21) at 25° and 35°, Todd's data fall off the correlation about 20% in the direction of low reaction rate.

The slope for such a plot contains as a factor the external dipole moment of a molecule such as it becomes

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(20) Amis, E. S., "Kinetics of Chemical Change in Solution", MacMillan Co., New York, 1949, p. 161.

(21) Maryott, A. A., and E. R. Smith, "Table of Dielectric Constants of Pure Liquids", National Bureau of Standards Circular, 514, (1951).

under the action of the polarization created by itself (22). The polarization a molecule can bring about in different solvents will depend on the shape of the solvent molecules and their specific dipolar field patterns. Since in these regards, acetone, acetonitrile, and nitromethane are not very similar, the only significance here attributed to this correlation is that it gives roughly correct results in the intermediate dielectric constant solvents. It does get worse at the lower dielectric constants in that the rate constant does not increase as much as the correlation predicts. Roughly, this means that as the average potential field of the solvent becomes less intense, particular dipolar groups of solvent molecules can make up part of the difference by moving more closely to the field of the reactants. Specific solvent effects become more pronounced such as the effect of water on the rates in this work, or the difference in rates in acetonitrile and in nitromethane where the effect due to dielectric constant is negligible.

Little can be learned from the enthalpies and entropies of activation because of their irregularities. It has been shown that for any equilibrium phenomena, changes of free energy with parameters, as when utilizing liquid models, will be more regular than the changes of enthalpies and entropies. This results from the necessity that

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(22) Harris, F. E., and B. J. Alder, Journal of Chemical Physics, 22, 1806 (1954).

$\partial F/\partial \alpha = 0$ while $\partial H/\partial \alpha$ and $\partial S/\partial \alpha = 0$, where α is any parameter representing a solution property such as..."volume or distribution of like and unlike pairs" (23). In other words, for any reasonable model or assumption, the errors due to the failures of the analogy, which accumulate in the enthalpy and entropy terms, tend to cancel in the free energy term. Consequently, we may look upon the unsystematic variations of the enthalpies and entropies of activation in this study as indications of poor assumptions which were made for systems at equilibrium. For example, we have assumed that the effect of the solvent on the rate constant is due to the changing of the activities of the reacting species relative to the activity of the activated complex with which they are in equilibrium. Such an assumption is implicit in any rate constant study based on the Eyring equation. Next we assumed that the solvent with the highest dielectric constant will bring about a lowering of the rate by binding the reactants, bromide ion and dipolar ester, more tightly than the ester- bromide ion complex. Such an assumption seems to be borne out by the rate constants. But trying to follow this trend in the tables of enthalpies and entropies of activation, we find that, for the succinate, the principal effect on changing the solvent lies in the entropy term. We could

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(23) Hildebrand, J. H., and R. L. Scott, "The Solubility of Non-electrolytes", 3rd edition, Reinhold Publishing Corporation, New York (1950), p. 135.

consider this to mean that the bromide ion is no more tightly bound to acetone than to nitromethane, that the factor of fifty, by which the rate constant was changed, resulted almost entirely from the probability of the reaction being less in nitromethane. In other words, acetone affords bromide ion about as much solvation energy as nitromethane, but there are more possible ways for bromide ion and the nitromethane to arrange themselves and avoid reaction. This interpretation is surprising, but there is still the glutarate to consider. We find practically the reverse trend. This time the enthalpy term accounts for the difference in rate constant in going from acetone to nitromethane. The two esters differ only in the additional methylene group in the glutarate, and we are unable to offer a suitable explanation for these solvent effects. Nevertheless, the ratios of the rate constants for all three esters are very regular, changing almost as 25 : 1 : 1/2 from acetone to acetonitrile to nitromethane at 25° and also at 35°.

Hildebrand's treatment (24) of solvent power in terms of a solubility parameter $\delta = (\Delta E/V)^{1/2}$, the square root of the cohesive energy density, ΔE being the heat of vaporization at constant volume and V being the molar volume, can be used to estimate the effect of the solvent

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(24) Ibid., Chap. 16.

on reaction rate. It was developed for non-electrolytes that conform to the demands of a regular solution; that is "...one in which orienting and chemical effects are absent, and in which the distributions and orientations are random just as in the ideal solution...We may expect, further, that a small correction should be applied to take care of the change in entropy accompanying change in volume, given by $(\partial S/\partial V)_T = (\partial P/\partial T)_V$..." (25).

The equation $\ln\frac{a_S}{a_A} = [\ln\Psi + \Psi_S(1-V/V_S) + V\Psi_S^2 (\delta-\delta_S)^2/RT] -$

$[\ln\Psi + \Psi_A(1-V/V_A) + V\Psi_A^2 (\delta-\delta_A)^2/RT]$

should give the activity ratio $\frac{a_S}{a_A}$ of a solute in two solutions S and A where the molar volume, volume fraction, and solubility parameter are V, Ψ, and δ for solute; V_S, Ψ_S, and δ_S for solvents; V_N, Ψ_N, and δ_N for solvent N. Solvents S, A, and N refer, respectively, to acetone, acetonitrile and nitromethane. Hildebrand considers $(\Delta H - RT)/V$ as the best estimate of cohesive energy density, where ΔH = enthalpy of vaporization and V = molar volume, and the geometric mean formula as the best rule for obtaining the cohesive energy density of mixtures. Therefore, the solubility parameter for solvents was taken = $[\frac{\Delta H - RT}{V}]^{1/2}$.

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(25) Ibid., p. 122.

Because δ is used just for solubility correlations, it is more practical than fundamental. Therefore, we may hope for only an order of magnitude correlation of the activity of bromide ion in different solvents using δ. This procedure is based on several assumptions: (1) The increase of cohesive energy of dipolar molecules as compared to analogous non-polar molecules is due largely to an increase in non-polar van der Waals forces and is due only to a lesser extent to dipole coupling forces. (2) The effect of an ionic charge being long range compared to that of a dipolar molecule does not change from solvent to solvent any more than the change of cohesive energy would predict. (3) The changes of ester molecules from solvent to solvent will be an order of magnitude less than that of the bromide ion, and since neither activity data nor heats of vaporization are available for these esters, there is no choice but to lump the ester solubility parameter effects in with the bromide ion effect.

Water at its boiling point has a cohesive energy which must be practically independent of orientation. The hydrogen bonds contribute to the cohesive energy without demanding a rigid structure; they can roll through large angles in vigorous libation without greatly changing the energy of the hydrogen bond. At 25° this would be less true, but the pure substance in the absence of solutes

which introduce specific packing and orientation requirements, should behave as simply a strongly cohering liquid; i.e., a regular solution. The bromide ion dissolved in acetone, acetonitrile, or nitromethane will be placed in the same scheme with Xenon and water because it, like they, would appear to satisfy the principal demand of the regular solution, in spite of its charge, because its attractions on near neighbors in the systems employed here is thought to be insensitive to the orientation of either them or itself. V will be taken = $\frac{4}{3}\pi r^3 N \times 10^{-24}$cc. where "r" is the crystal radius for bromide ion in $\mathring{A}$. V = 18 cc. and $\ln\frac{\Psi_S}{\Psi_A}$ is negligible. δ must be divorced from the idea of evaporation and compared by crude analogy with Xenon and water. This is in accord with our assumption (2) by which we consider an ion in solution very much like a strongly dipolar molecule. Fundamentally, a dipole consists of two separated electric charges. In solution it is commonly known that only those dipoles which place a charge "on the surface" of a molecule (26) have much effect. Now a surface charge is not different at close range whether it came from another part of the molecule (and therefore has an equal opposite charge behind it) or whether it is simply part of an extra charge spread

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(26) Bernal, J. D., Transactions of the Faraday Society, 33, 210 (1937).

around by its mutual repulsion. At long range there is a very real difference, but only short range forces seem to be important in determining solution interactions. We assume, then, that the strong dipole model of bromide ion will suffice for comparative purposes, and by assumption (1) we have already discussed the use of strongly dipolar substances in the same scheme with non-dipolar substances. Hildebrand (27) considers that the δ for water obtained from solubility measurements in hydrocarbons, 22.0-24.8, compares so closely with $\delta = [(\Delta H - RT)/V]^{1/2} = 23.5$ $(cal./cc.)^{1/2}$ at 25° that only a remarkable coincidence could have been responsible. From our point of view, there is not so much difference of the cohesion between pure water at room temperature and that of xenon at room temperature except for the magnitude of it. The ability of water to be oriented by strong fields and to be attracted into small spaces by irregularly shaped solutes are, of course, differences in kind, but in hydrocarbons such effects are not as important energy wise as cohesion in determining solubility and activity.

Xenon is the same size as bromide ion but contains no electronic charge on its surface. Water is only a little smaller than bromide ion, and contains two partial electronic negative charges on its surface. We attribute

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(27) Hildebrand, op. cit., pp. 266, 8.

the extra cohesive energy of water, above that of xenon ($\delta = 8.0$) to the presence of the two negative partial electronic charges on its surface giving large London dispersion forces and to the many possible attractive arrangements of its negative charges and protons. Thus the contribution to the solubility parameter of the unsymmetrical charge distribution is $24 - 8 = 16\ (\text{cal./cc.})^{1/2}$. Bromide ion has one extra electron, and, even though the comparison between its contribution of the strong dipoles in water to its solubility parameter cannot even be approximated, it might prove instructive to see what empirical value of δ for bromide ion would satisfy the Hildebrand equation as if all the difference in rate constants from solvent to solvent was due to change in solvation energy of the bromide ion. It is not easy to separate out the effect of the solvent on the bromide ion-ester complex because there is no data on even the ΔE of vaporization of the esters. We could set up simultaneous equations to solve for the best set of δ's for the bromide ion, the three esters and their three activated complexes, but it would not prove anything because the enthalpies and entropies of activation have already demonstrated the importance of entropy effects from ester to ester such as are not allowed for in the Hildebrand equation. Roughly speaking, the effect

of the solvent on the bromide ion part of the activated complex ought to parallel its effect on the bromide ion, but it should be smaller due to the ionic charge being diffused over a larger surface. The effect of the solvent on the activated complex due to its ester molecule ought to parallel its effect on the ester molecule, but not be much different in magnitude because the esters used in this work are of approximately equal polarizabilities.

$\underline{25^\circ\ C.}$ $\delta(CH_3NO_2)$ = 12.6 (28) V = 54 cc./mole

$\delta(CH_3CN)$ = 12.3 (29)

$\delta(CH_3COCH_3)$ = 9.8 (29)

$$\ln \frac{a \text{ in } S}{a \text{ in } A} = \ln \frac{\Psi \text{ in } S}{\Psi \text{ in } A} + V\left(\frac{1}{V_A} - \frac{1}{V_S}\right) + \frac{V}{RT}\left[\Psi_S^2(\delta - \delta_S)^2 - \Psi_A^2(\delta - \delta_A)^2\right]$$

Assume: Ψ in S = Ψ in A

$\Psi_S = \Psi_A = 1$ i.e., solutions very dilute in bromide ion.

$$(\delta - \delta_S)^2 - (\delta - \delta_A)^2 = 2\delta(\delta_A - \delta_S) + \delta_S^2 - \delta_A^2$$

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(28) Hildebrand, op. cit., p. 438.

(29) Dreisbach, R. R., "Physical Properties of Chemical Substances", Vol. 2, Cox Chart Families 19 and 21, Dow Chemical Company, Midland, Michigan, 1955.

$$\ln \frac{a \text{ in } S}{a \text{ in } A} = 0 + 18\left(\frac{1}{52.5} - \frac{1}{74}\right) + \frac{18}{596}\left(2 \times \delta \times 2.5 + 9.8^2 - 12.3^2\right)$$

$\ln 25 = 3.22$ and $\delta = 32$

solving for $\ln \frac{a \text{ in } N}{a \text{ in } A}$ using $\delta = 32$

$\frac{a \text{ in } N}{a \text{ in } A} = 0.72$ instead of 0.54 as observed.

The polar nature of bromide ion, then, has given it a solubility parameter of 32, 8 for the atom, and 24 for its ionic charge according to our assumptions. We hasten to add that the cohesive energy approach, as extended here, is better than no prediction at all, but without spherical symmetry of the solute there would be very little reason to assume the regular solution model. It would be interesting to have more extensive data to see whether the δ of bromide ion is constant enough to be really useful.

The general conclusion can be drawn that for the systems studied, the direct solvent effects on reactivity have been roughly correlated, and for relative free energy effects the systems chosen are suitable; but to distinguish between the strengths of interactions and the effects of probability, the solvents should be altered more gently. It seems desirable to use mixtures of these three solvents to achieve a gradual transition from acetone to acetonitrile, acetone to nitromethane, and acetonitrile to nitromethane. There would, of course, be the added complications

of specific solvent-solvent interactions. But even these could probably be turned to account in identifying the nature of the effects of solvents on reaction rates.

D. Direct ester structure effect.--The second trend which was established was the increase of the rate constant with increased polarity of the ester. The rate constants for the caproate, the glutarate and succinate varied as (0.186 ± 0.025) : 1.00 : 1.28 ± 0.18 in all three solvents including both temperatures. Roughly, the diesters reacted five times as fast as the monoester. This trend can be extended by noting that the rate constant for isobutyl bromide in acetone at 25° is given as .0057 x 10^{-3} l./mole sec. for 0.024 M LiBr.(30) Using an ionization constant of 1.13 x 10^{-3} M for lithium bromide in dry acetone (4) and neglecting the rate due to lithium bromide molecules, we find:

$$0.0057 \times 10^{-3} \frac{0.024 \text{ M (gross LiBr)}}{0.0047 \text{ M (Br)}} = 0.029 \times 10^{-3} \text{ l./mol.sec.}$$

which is .000029/.00367 = 0.0079 as fast as the glutarate. This value could not be corrected for the effect of the concentration of the butyl bromide, if any, since in de la Mare's treatment this effect was lumped into a "salt effect" along with the ionization constant of lithium bromide. But the comparison is consistent, and we find the rate constants of the series alkyl : monoester : diester to compare as 0.008 (in acetone only) : 0.2 : 1.0. This trend suggests

that the polar effect of ester groups, withdrawing charge from the carbon atom on which the racemization takes place, permits the products to form the transition state complex with a smaller increase of free energy. Once again we are unable to get a clear interpretation of the enthalpies and entropies of activation; however, most of these quantities point toward the trend being primarily an entropy effect, except for the caproate in nitromethane where the ester concentration extrapolation may have been in error. Thus it would appear that the function of the ester groups is to increase the probability of any collision being followed by reaction. This could be thought of as the attraction of the bromide ion to the vicinity of the c-Br dipole by the polar ester groups. The activation energy of de la Mare's measurements on isobutyl bromide was right in line with those found in this work, 18.9 k.cal./mole.

The temperature effect on direct ester structure effect also must be dealt with only as a free energy change. Surprisingly enough, the increase of temperature from 25° to 35° increased the relative rate constants of all nine systems by a factor of 2.5 ± 0.4 except for the caproate which increased by 1.9 and 3.1 in acetonitrile and nitromethane, respectively.

Thus even with important ester concentration effects and no generally applicable correlating equation, the

solvent structure effects, the ester structure effects and the temperature effects have been dealt with in terms of free energy, and we suspect that improper extrapolations to the rate constants at zero ester concentrations have had no small part in the failure of interpretations involving the enthalpies and entropies of activation. Although it would be possible to solve for two solubility parameters for each ester as was done with the bromide ion, a consideration of the ester concentration effect suggests that these solvent-ester mixtures are not regular. If good molar volume data and good heat of vaporization data were available, the regular solution equation could be used to examine the non-random distribution of solute.

E. Ester concentration effects and clustering.--To explain a variation in a second order rate constant with the concentration of one of its reactants, it would be sufficient to establish a non-homogeneous distribution of the two reactants, thus the product of the concentrations of the bromide and esters molecules could be either greater or smaller than the stoichiometric product, depending on whether the two reactants tended to cluster together or whether one or both of them tended to form clusters which excluded the other. Thus it is here proposed to introduce the concept of inhomogeneity of ester distribution in solution to account for the ester concentration effects. It

will be postulated that molecules of different free energy of solution (resulting from the combined attractions of polar bonds and van der Waals bonds) will not be randomly distributed in a single homogeneous solution as they would be in a regular solution, but, rather, will form clusters. To employ such an assumption, it would help to review the case for clustering in solution as a general phenomenon. Then we should interpret the actual ester concentration effect data and notice whether the inter-molecular attractions necessary to explain the data do violence to well established chemistry.

Scatchard, in a review article (31), has considered clustering as a foregone conclusion. "Of course the distribution of the molecules in a solution will not be random if there is a change of energy when contact between two A molecules and that between two B molecules is replaced by two contacts between A and B molecules." Perhaps this statement should have been made in terms of the free energy change that would result. It is well known, for example, that entropy effects can be greater than those of enthalpy. Thus the excess free energy of mixing (32) tetraethylmethane in n-octane at 50° is a positive quantity with a maximum at

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(31) Scatchard, G., Chemical Reviews, 44, 7 (1949).

(32) Prigogine, I. and R. Defay, "Chemical Thermodynamics", Chap. 24, Longmans, Green and Co., London, 1954.

about 0.5 mole fraction in spite of the excess enthalpy of mixing being negative. It is surmised that the heat evolved by the decrease of internal energy on mixing cannot have come from the velocity of the molecules but from the other modes of motion. If the mixing has diminished their velocities in the bulk it seems reasonable that the velocities of those which must escape to become vapor would likewise be diminished. Thus would the pressure of the vapor be made less, contrary to the measured excess of vapor pressure over that predicted by Raoult's law. The alternative would seem to assume some mechanism to convert energy from other modes to translation just prior to flight. Collision being the principal energy transferring mechanism, we are still left needing augmented translation in the bulk of the mixture. Solutions of n-heptane and n-hexadecane at 20° behave just oppositely. The excess free energy of mixing is negative in spite of a positive enthalpy of mixing. Solutions of 2-2-4 trimethyl pentane and hexadecane have practically no excess free energy of mixing because the positive excess enthalpy of mixing of about 50 cal./mole at 0.5 mole fraction is almost cancelled by an entropy effect of like magnitude. The excess molar free energy uses ΔF (ideal mix) = $RTX_1 \ln X_1 + RTX_1 \ln X_1$ as its ideal mixture molar free energy for any binary solution by which to compare the actual molar free energy. ΔF (mix) = $RTX_1 \ln \gamma_1 X_1$ +

$RTX_2 \ln \gamma_2 X_2$. The excess of the actual mixture, $F^E = RT\ln\gamma_1 + RT\ln\gamma_2$, is stated in terms of the mole fraction activity coefficients γ_1 and γ_2. The excess enthalpy of mixing is

$$H^E = -RT^2 \left(X_1 \frac{\partial \ln \gamma_1}{\partial T} + X_2 \frac{\partial \ln \gamma_2}{\partial T}\right) .$$

It is concluded that unless γ_1 and γ_2 are not only unity but also invariant with temperature that the modes of motion have been altered by the process of mixing. We might expect also that the distribution of the molecules will not be random. Quoting from Hildebrand (33), "The statistical model from which the regular solution equations were deduced envisages solutions in which thermal motion is sufficient to produce a completely random distribution of solvent and solute molecules. Even though the interaction between different kinds of molecules is assumed to be different in order to account for non-zero heats of mixing, the tendency of these energy differences to cause segregation of the solution into clusters of like molecules is ignored. This leads to an apparent contradiction, since this clustering tendency must be the driving force which results in ultimate gross separation into two phases." Most of the work on systems in the critical state has dealt with pure substances at the vapor-liquid transition. Clustering for this situa-

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(33) Hildebrand, J. H., "Annual Reviews of Physical Chemistry", Vol. I, Annual Reviews, Inc., Stanford, California, 1950, Chap. I.

tion has been well established by light scattering experiments (34).

The statistical formulation of clustering has been presented in terms of a "distribution function" (35) which permits the calculation of all thermodynamic functions in terms of the probability of a configuration, at least in principle. Since all possible coordinates are included, this formulation is practically free of any model. The first success of this treatment was the prediction of horizontal isotherms on the pressure volume diagram of a substance just above its critical temperature. As observed by Maass and co-workers (36), the critical region was characterized by a density distribution as shown by making a vertical buoyancy traverse at temperatures just above that at which the last meniscus was observed. This is a clear example of clustering in the gas phase. The failure of a distinctive phase separation to appear is analogous to the case of liquids above the critical solution temperature. O. K. Rice has reviewed this analogy (37) and sug-

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(34) Zimm, B. H., Journal of Chemical Physics, 21, 1934 (1953).

(35) McMillan, W. G. and J. E. Mayer, Journal of Chemical Physics, 13, 276 (1945).

(36) McIntosh, R. L., J. R. Dacey, and O. Maass, Canadian Journal of Research, B17, 206, 241 (1939).

(37) Rice, O. K., Journal of Chemical Physics, 15, 314 (1947).

gested that differential total vapor pressure measurements and surface tension measurements should be made to show up clustering in binary solutions along isotherms just above critical solution temperature. Concerning a substance in such a confused state, typified by the absence of a meniscus along with nearly flat pressure-volume isotherms, Rice has described it (38) as "...spongy, complexly interconnected mass of variable density. The process of condensation will now consist of the compression of the spongy mass, reducing the...interconnected regions of low density to the status of disconnected bubbles in the liquid." Bhagavantam (39) described the light scattering by liquids due to chance fluctuations of density and by solutions due to the combined fluctuations of density and concentrations. The presence of clustering and even some rough idea of its extent should be obtainable from light scattering experiments. Light and microwave absorption cannot lead to any unique indications of liquid clustering because the intermolecular transitions between clusters and the surrounding solution occur with such low energy that the effects simply modify the absorptions caused by rotational and vibrational transitions. X-ray scattering shows up liquid structure

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(38) Rice, O. K., Chemical Reviews, 44, 69 (1949).

(39) Bhagavantam, S., "Scattering of Light and the Raman Effect", Andhra University, Waltair, India, 1940.

insofar as the average number of nearest neighbors is of interest, but even in a pure liquid the absence of long range order and the diversity of short range order makes the scattering so ill defined as to confuse the interpretation. Sound waves have been used to elucidate liquid structure but mostly from the standpoint of sound dispersion itself. Dilatational viscosities have been determined which measure the resistance of a liquid to divergent flow in the absence of shear; i.e., sound waves alternately compress and rarify a medium during their passage through it, and the phase lag between the pressure wave and the intermolecular rearrangements cause an absorption of the sound energy. If the sonic frequency could be continuously varied and the absorption measured, any mechanical frequency equal to the relaxation frequency of a particular intermolecular configuration would have a corresponding absorption maximum. It is the relative independence of the response of an individual cluster that is sought, and the absence of long range order might permit it. Thus it would be expected that a mechanical stress would force surrounding solvent molecules into solute clusters and, in the relaxation following, the solute cluster would reform and dissipate its stored potential energy into kinetic energy of the intruders which would quickly become random. Just how other modes of molecular motion would participate

in such a divergent flow is not clear. But it does seem that no unique absorption peaks would be possible if a given pulse included too many clusters in one stress wave; there would be an excessively broad range of resonant responses and no sharp absorption by any. In such a situation, it would still be valuable to correlate the amount of absorption with the concentration of solute and compare it with a derived equation.

Let us now consider the extension of this clustering to the analogous situation of changes of structure in a liquid mixture, noting the difference as related to intermolecular forces. When water is formed from ice at 0° there are observable remnants of the ice-like configuration still present in the midst of another tetrahedral configuration in which four water molecules surround one in the manner of quartz (40). It is the somewhat open lattice of such clusters that gives water its density maximum at 4°, because as the temperature increases, these ice-like clusters "melt" and form more quartz-like tetrahedral arrangements which are more densely packed; hence the increase in density. Water molecules have a "dipole moment", but it is not important as a single entity. The important aspect of the polarity of water molecules is that it is manifest as four charged spots, two near the hydrogen

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(40) Bernal, J. D., and R. Fowler, Journal of Chemical Physics, 1, 515 (1933).

nuclei of positive charge and two others of negative charge, all four disposed over the nearly spherical surface of the water molecule approximately as the points of a tetrahedron. This gives water at room temperature its structure and exemplifies the irrelevance of the average polarity in the determination of the way a substance will arrange its molecules in a condensed phase. In gases, the forces of attraction and repulsion that cause deviation from the perfect gas law are called Van der Waals' forces, and these are the same forces which together with the attractions of dipoles and charges, hold molecules together in liquids. The decrease of attractive forces with distance depends on their origin, varying from the inverse second power for two charged particles to the inverse sixth power for the second order perturbation interaction of the electron clouds (41). The strength of repulsive forces decreases according to the inverse power of the distance anywhere from the tenth to the thirteenth as arrived at empirically (23). Thus it is not difficult to see how two different phases could be in equilibrium with such forces: one, the gas phase, in which only a small fraction of its molecules will at any one time be within the attractive fields of neighbors; the other, the liquid phase, made up of cohering clusters, must lose a fraction

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(41) Morgenau, H., Reviews of Modern Physics, 11, 1 (1939).

of its members to its vapor phase when occasionally the component of the translational energy of a few molecules in the direction perpendicular to the surface of the liquid exceeds the escape velocity. The difference in the two phases is easily attributed to the near absence of cohering molecules in the one and the absence of independent molecules in the other, all because of the very weak attractions between molecules already separated many molecular diameters, and the existence of intense attractions between molecules already packed so closely together that the movement of a molecule away from one neighbor's attractive field brings it within that of another. The explanation of the phenomenon of different condensed phases at equilibrium, where there is no great change of distance between the molecules in passing from one to the other, has the problem of describing alterations in the potential pattern. This is very difficult because of the sensitivity of the potential to the intermolecular configuration, i.e., the way the molecules are clustered. Two liquid phases at equilibrium must have arrangements of molecules in one structurally similar to the other phase so that, given a change of temperature, more of the second phase can be formed on the floating templates already present in the first phase; this seems reasonable enough but elusive. Is it a case of pure conjecture, or is there some basis

for judging the existence and properties of such clusters? The phenomenon of critical condensation of a vapor is valuable only as an analogy to help point out what to look for. The interest of Rice has been to point out that the total vapor pressure isotherms should be relatively constant over a range of compositions, just above the critical solution temperature, in analogy with the corresponding behavior of pure substances along isotherms just about their critical temperatures. If clustering were extensive enough, the mixture would be "buffered" against changes in free energy; hence, partial molal fugacities and partial pressures would remain constant. Following the treatment described above (32), we would expect one good approach would be to measure enthalpies of mixing using calorimetry and free energies of mixing using total vapor pressures, along isotherms in mixtures in which reaction rate measurements have indicated clustering. Entropy effects along the same isotherms are obtained by the difference $\Delta H - \Delta F = T\Delta S$. Valuable results, too, might be obtained by vapor pressure measurements at extreme dilution measuring deviations from Raoult's law. If clustering were pronounced, then deviations should show up at mole fractions of solvent greater than 0.9.

It should be kept in mind that vapor pressure measurements, like any measurements of free energy effects, are

unlikely to show up enthalpy and entropy effects following the outline mentioned previously. For any single line of attack, the difficulty of interpretation can be stated another way. It is difficult to distinguish between "chemical" effects and "physical" effects. To distinguish between chemical and physical causes of deviations from Raoult's law it is sometimes noted that chemical forces imply saturation of the force itself while physical forces do not. Acetic acid vapor at room temperature is almost completely dimerized, but that brings the associating process to an end--the forces of attraction are saturated. The formation of trimers would result from physical forces such as describe Van der Waals deviations from the perfect gas law. A similar case of saturation exists in the equilibrium between gaseous NO_2 and N_2O_4. But it is often impossible to distinguish between chemical and physical forces by taking only one kind of data. A case in point (42) is the impossibility, at this time, of ascribing the empirical constants derived by conductance data to one or the other of these effects. Whether the salts be weak or simply impeded in their migration by electrostatic forces remains an ambiguous question. Therefore, it would be the better route to combine the attack and measure isothermal

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(42) Harned, H. S., and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions", A.C.S. Monograph, Reinhold Publishing Corporation, 1950, p. 159.

heat effects for the same mixture. Utilizing Hildebrand's regular solution equation for that part of the activity due to enthalpy effects and those entropy effects due to different sizes of molecules, the remainder of the total entropy effect, if any, could be attributed to chemical clustering.

In acetone the caproate had the greatest concentration effect, the succinate and glutarate had less. At 25° the glutarate was more effective than the succinate while at 35° the reverse obtained. We are led to consider the least polar ester as the most completely clustered. The exchange of the concentration effects of the succinate and glutarate with temperature could be due to the extra methylene group in the glutarate. At 25° the carbomethoxyl groups could, by using the glutarate's greater flexibility, cancel its own electrostatic fields by intramolecular coupling achieving a quadrupole configuration. Having less electrostatic energy, the individual glutarate molecules would be less polar and acetone would solvate it less than the succinate; hence, the glutarate would have a greater tendency to segregate to itself, away from the acetone. At 35°, since the reverse order was observed, we are led to surmise that the increase in temperature has caused the two carbomethoxyl groups to decouple like linear high polymer molecules uncoiling. Since these effects lower the rate

constant by factors up to two or more, the corresponding changes in ΔF would be up to $RT\ln(1/2) = -420$ cal./g.mole. If ester clustering were causing this, then, there should be measurable excess free energies of solutions of esters and acetone on the order of hundreds of calories per mole of mixture. It would not be surprising to find that there was a small or positive excess enthalpy of mixing and that the negative excess free energy is caused by a large positive excess entropy effect. These effects are large enough to be measured experimentally. The heat effects at constant pressure and temperature give H^E, and total vapor pressure isotherms give F^E.

Since clustering has, up until now, been primarily associated with incipient phase separation, it would be desirable to see if the caproate formed two phases in acetone at temperatures not far removed from 25°. But even if no actual phase separation occurred, it is still reasonable to assume that clusters could form, because at temperatures just above the critical solution temperature there must still be clusters of different composition present, one type richer in one component and the other type richer in the other component. Otherwise, how could total pressure isotherms remain nearly constant over a range of compositions, however short? It is here suggested that "dissolved phase" is a proper description of a "cluster"

when they are large, but there is no boundary between solutions containing the "dissolved phase" type and solutions which simply display deviations in entropy of mixing from that of ideal, Raoult's law solutions.

In acetonitrile the caproate once again had the greatest concentration effect but in the opposite sense; the rate constant increased with ester concentration at 35°. This leads to the conclusion that bromide ions are tending to segregate with the ester molecules. It is to be noted that TeaBr was more soluble in acetonitrile than in acetone and was apparently a strong electrolyte up to 0.1 M. Since we can explain only a small part of this difference (TeaBr in acetone saturated at about 0.006 M, $K = 15 \times 10^{-3}$) on the difference in dielectric constant we surmise that specific solvent effects, probably hydrogen bonding of the bromide ion, have made the difference. Noting that the dipole moment of the acetonitrile calculated for the liquid is smaller than that obtained from data of its vapor (43) we interpret this to mean that acetonitrile molecules are associated contra-wise to some extent; i.e., head to head. In contra-association, the dipoles are arranged into quadrapoles with a consequent loss in electrostatic potential energy. The effect of a dissolved bromide ion solvated specifically by acetonitrile

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(43) Böttcher, C. J. F., Physica, 6, 59 (1939).

molecules would be to present a sphere whose surface is made up of methyl groups to the rest of the solvent. This certainly parallels the picture of bromide ions in water; the bromide ion is said (44) to create disorder in the solvent by making it difficult or impossible for contiguous solvent molecules to take part in the regular structure of the solvent. Since the structure of pure solvent arrangements has to be broken to form ester clusters, consider the possibility of an overall decrease in the free energy of the mixture by the formation of clusters of bromide ions, ester molecules, and acetonitrile molecules oriented in the clusters with their dipoles toward bromide ions and their methyl groups toward an ester molecule. Assuming that ester-solvent clustering will occur, this would certainly minimize the number of disordered acetonitrile molecules, and even if only a very small fraction of the bromide ions were brought into such an arrangement, an increased opportunity for reaction would result. Acetone did not show such an effect, nor would it be expected. It's dipole is known (45) to be buried deep enough for its molecules to

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(44) Gurney, R. W., "Ionic Processes in Solution", McGraw-Hill Publishing Company, New York, 1953.

(45) Harris, F. E. and B. J. Alder, Journal of Chemical Physics, 21, 1031-8 (1953).

rotate independently (Kirkwood's g factor is unity for acetone). Neither does nitromethane show a positive ester concentration effect. It is known to be a Haentsch acid and, consequently, a pair of nitromethane molecules could be helped in their contra-association (43) by an intervening bromide ion. Two ionized nitromethanes and a bromide ion could fit together and present methylene groups with partial negative charges to the surrounding solvent, preserving, or perhaps even aiding, the polar nature of the solution. It will be remembered that the extrapolated rate constants were lower in nitromethane than in acetonitrile although the dielectric constants of the two solvents are almost identical. Hence, the more complete interaction of nitromethane with bromide ion, as postulated to explain the difference in ester concentration effects between nitromethane and acetonitrile, is also in accord with the difference in the direct solvent effects on these reactions.

At 25° for neither nitromethane nor acetonitrile was there any ester concentration effect. It seems probable that specific solvent-ester interactions, which are destroyed by increased molecular rotations between 25° and 35°, help the ester molecules disperse at 25°. The falling off of the solubility of some salts in water is probably due to a similar phenomenon. Above 40°, water molecules are thought

to rotate on an axis (46), which bisects the H-O-H angle making it less able to enter into hydrogen bonding.

The interaction of non-polar solutes with polar solvents such that the greater the polarity of the solvent the greater the dispersal of the solute, is another aspect of solvent effect that has been interpreted only with difficulty. The loss of entropy of non-polar gases on dissolving (47) indicates a less random configuration of water molecules. Robinson and Stokes (48) consider this "...as an increase in the average life of the shortrange tetrahedral configurations, due to the reluctance of the solute particles to get out of the way." This passage illustrates the lengths to which authors will go to avoid imputing appreciable cohesion between water and a molecule with only Van der Waals forces. Let us assume that rare gas molecules are bound by Van der Waals forces to water molecules and that that explains why they dissolved in the first place and remained to lengthen the transitory existence of life in a water tetrahedron. In support of this assumption (46) "...the extra entropy loss is greatest for the heaviest and largest solute molecules, such as radon and chloroform."

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(46) Magat, M., Transactions of the Faraday Society, 33, 114 (1937).

(47) Frank, H. S. and M. W. Evans, Journal of Chemical Physics, 13, 507 (1945).

(48) Robinson, R. A. and R. H. Stokes, "Electrolyte Solutions", Academic Press Inc., 1955, p. 14.

These are the conditions for strongest Van der Waals forces per solute molecule corresponding to a greater number of electrons for dispersion, and a greater surface for interaction. It was noted that the effect increased as the temperature lowered. This reminds one of the increase in the familiar maximum in the viscosity of acetone-water mixtures as the temperature is lowered. Both instances show that the degree of alignment of water molecules in orientation-sensitive structures makes possible this negative excess entropy. In other words, the more orderly the molecules of water are arranged, the greater the increase in that orderliness which can be brought about by the presence of non-polar attractions. Consider the possibility that the persistence of a particular five-membered structure (one water molecule surrounded tetrahedrally by four others) might be increased by the presence of a molecule which could hold one or more polar water molecules on its surface without the difficult orientation requirements which characterized the polar water molecule or molecules which it replaced.

These observations can be summarized by saying that polar interaction energy depends on Van der Waals interaction energy. The reverse was stated in the consideration of the nature of the cohesion of water at its normal boiling point; i.e., Van der Waals interaction energy is high

because of the polar nature of the molecules. Returning to the question of ester clustering, we can now deduce the cause of the clustering disappearing in acetonitrile and nitromethane going from 35° to 25°, while in acetone it increased over the same change in temperature. Acetone is structureless as a pure solvent, having a Kirkwood g-factor of unity, indicating no orientation interdependence; hence, its structure could not be increased by non-polar binding; i.e., it cannot lose potential energy in this way. At higher temperatures, the greater molecular motions simply decrease the ability of the ester to resist thermal agitation. The succinate did not follow this trend, but showed a slight increase in ester concentration effect with rise in temperature. This suggests that the cohesive energy density of acetone has fallen faster than that of the succinate over the temperature interval. Heretofore, this relative change in cohesive energy density of ester with temperature has been left out of the discussion. It is not possible to discuss it without heat of vaporization data and molar volume data over the temperature range at hand, and therefore, it simply is an unknown in all of these ester considerations.

F. The ionization constant for tetrabutylammoniumbromide in acetone.--It was found that to correlate the pseudo-first order rate constants for the succinate in acetone,

the ionization constant for tetrabutylammoniumbromide, K(TbaBr), had to be taken equal to 17 x 10^{-3} mol./l. It was possible, using the procedure devised, to fit the data throughout the range of salt concentration in such a way as to note whether a change of K would be necessary from concentrated to dilute solution. Unfortunately, TbaBr was used solely to see if the derived bromide ion rate constant using tetraethylammoniumbromide would fit the TbaBr data. Since it did, there was no further interest in TbaBr at the time. Now it is clear that the limited solubility of TeaBr (about 6 mM at 25° saturated acetone), by holding the maximum concentration of bromide down, limited the range of the studies so much that a constant K could be forced on the empirical curve even if there were an appreciable change in K actually. It is concluded that future work could well be carried out using the butyl salt instead of the ethyl.

No outright assertion as to the accuracy of K as derived for the work here can be justified in the light of the limited range of concentrations of salt used, but if measurements of high precision gave a K from rate data distinctly different from one obtained from conductance data, the burden of proof would lie just as much on the conductance data as on the rate data. The difficulty of interpreting empirically derived conductance constants

was shown above. The effects due to higher ionic forces cannot be distinguished from those due to association of the ions. In a reaction, however, if the ion does not exist, it cannot react. The fact that it might cluster with the other reactant is not to be ignored, but in acetone the presence of appreciable concentrations of ester lowered the rate, and since the ester molecules have been shown to be clustering, the bromide ions must not have clustered. Nor are changes in the bulk properties of the solvent to be ignored. But at 5 mM salt the ions are separated 60 or 70 Å on an average and this seems to be too far for the change in solvent necessary to increase an ionization constant by a factor of four or five. Frashier's work, as described in the Introduction, showed that a change of LiBr concentration from 1.044 mM to 20.03 mM did not change the ester concentration effect any. Indirectly this indicates that the solvent did not change appreciably. The ester is present in a concentration of 0.13 M in most of the runs made, giving the ester molecules a bulk average separation of more than 20 Å. The absence of rotational structure in acetone, moreover, leads us to doubt any change of the acetone due to the dissolved ester.

In future work, since it has been shown that the salt molecule does not catalyze the racemization of the succinate in acetone either at 25° or at 35°, K could be

investigated with more assurance. It is believed that rate data provide a good basis for interpreting conductance data, and once more we conclude that different approaches will clarify the nature of solutions much better than more work along one particular approach.

CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS

A. Conclusions

1. In polar solvents, the less polar the solute the more it clusters.
2. In polar solvents it is possible for the more polar reactant to have the larger rate constant with an ion.
3. The value of ionization constants as derived from conductance data are not necessarily precise for use in reaction rate work.
4. Solutions of highly polar solutes in polar solvents can form solutions that are regular, except for size differences, only if hydrogen bonding or other specific solvent effects are practically non-existent.
5. Polar forces, dipolar forces, and non-polar forces produce solution effects by interdependent action.
   a. Polar molecules have larger Van der Waals forces than isoelectronic molecules of the same molecular volume.
   b. London dispersion forces between a non-polar solute and a polar solvent can increase the orientation structure of the solvent.

B. Recommendations

1. The dependence on the rate constant of the racemization of methyl α-bromoisocaproate and dimethyl α-bromoglutarate by tetraethylammoniumbromide in acetonitrile should be determined over a wide range of ester concentrations at several levels of salt concentration.
2. Molar volumes and heats of vaporization should be measured for dimethyl α-bromosuccinate, dimethyl α-bromoglutarate and methyl α-bromoisocaproate.
3. Total vapor pressure and heats of mixing should be determined for all nine combinations of acetone, acetonitrile, nitromethane, dimethyl α-bromosuccinate, dimethyl α-bromoglutarate and methyl α-bromocaproate.
4. Tetrabutylammoniumbromide should be used to extend the rates up to 1.5 l./mole sec.
5. The reactions in mixtures of acetone, acetonitrile, and nitromethane should be run to vary the solvent effect more continuously.
6. The ester concentration effects should be studied closely to better examine its change with temperature.
7. Tetraalkylammoniumbromides with larger alkyl groups should be used in solvents with dielectric constants lower than acetone, such as higher ketones and hydrocarbons to attempt racemizations.

APPENDIX

APPENDIX I

Fitting $k = k_1[\frac{K}{2}(\sqrt{1 + 4c/K} - 1)] + k_2[c-\frac{K}{2}(\sqrt{1 + 4c/K} - 1)]$ to observed pairs (k, c) solving for K, k_1 and k_2.

1. Draw a first approximation curve of k vs. c taking into account:
   a. (d^2k/dc^2) is negative for all values of c; its magnitude is greatest at c = 0 and falls smoothly toward zero at increasing values of c.
   b. (dk/dc) is positive for all values of c; in consequence of a, its value is a maximum at c = 0 and falls smoothly as c increases; its final value is k_2 at indefinitely large c.
2. Plot graphically determined slopes of the empirical curve drawn in 1 at closely spaced regular intervals of c as a function of c. If this plot of $(dk/dc)_{xpt.}$ vs. c does not conform to 1. b., repeat 1 drawing a second approximation curve of k vs. c. Continue 1 and 2 until a good fit is obtained.
3. Obtain k_1 by noting $k_1 = \lim(dk/dc)$ at c = 0.
4. On a separate graph plot $(dk/dc)/k_1$ vs. c where (dk/dc) is taken from the plot made in 2.

5. Obtain an approximation of K by noting:

$$\frac{K}{2} = \frac{k_1}{\lim(-d^2k/dc^2)_{c=0}} - \frac{k_2}{\lim(-d^2k/dc^2)_{c=0}}$$

6. Estimate k_2 by plotting $k/[Br^-]$ as a function of $[Br^-]$ and noting that a straight line should result with a slope of k_2/K. To calculate $[Br^-]$ from c use the approximate K found in 5.

7. On the graph used in 4 plot curves of $1/\sqrt{1 + 4c/k}$ vs. c, each one for a particular trial value of K close to the K found in 5.

8. The curve plotted in 4 should follow closely some curve plotted in 6 at low concentrations of c and should exceed it for higher values of c by the difference $\frac{k_2}{k_1}(1 - 1/\sqrt{1 + 4c/K})$.

9. At sufficiently high c, K will change and multiions may form adding reaction paths.

The equations needed for the foregoing analysis are derived below.

$$K = \frac{[Br^-]^2}{c - [Br^-]}$$

$$Kc - K[Br^-] = [Br^-]^2$$

$$[Br^-]^2 + K[Br^-] - Kc = 0$$

$$[Br^-] = -\frac{K}{2} \pm \frac{1}{2}\sqrt{K^2 + 4Kc} \qquad (1)$$

$$= \frac{K}{2}\left(\pm\sqrt{1 + 4c/K} - 1\right)$$

$$= \frac{K}{2}\left(\sqrt{1 + 4c/K} - 1\right)$$ since neither C, $[Br^-]$ nor K can be negative.

$$k = k_1(Br^-) + k_2(c - (Br^-))$$

$$\frac{dk}{dc} = k_1 \frac{d}{dc}[Br^-] + k_2 - k_2 \frac{d}{dc}[Br^-]$$

$$[Br^-] = \frac{K}{2}\left(\sqrt{1 + 4c/K} - 1\right)$$

Substitute using equation (1)

$$\frac{d}{dc}[Br^-] = \frac{K}{2} \cdot \frac{1}{2} \frac{4/K}{\sqrt{(1 + 4c/K)}}$$

$$\frac{dk}{dc} = (k_1 - k_2) \frac{1}{\sqrt{(1 + 4c/K)}} + k_2$$

$$\lim\left(\frac{dk}{dc}\right)_{c=0} = k_1 \qquad (2)$$

$$\frac{1}{k_1}\frac{dk}{dc} = \left(\frac{k_1 - k_2}{k_1}\right)\frac{1}{\sqrt{(1 + 4c/K)}} + \frac{k_2}{k_1}$$

$$= \frac{1}{\sqrt{(1 + 4c/K)}} + \frac{k_2}{k_1}\left(1 - \frac{1}{\sqrt{(1 + 4c/K)}}\right)$$

$$\left(\frac{1}{k_1}\frac{dk}{dc} - \frac{1}{\sqrt{(1 + 4c/K)}}\right) = \frac{k_2}{k_1}\left(1 - \frac{1}{\sqrt{(1 + 4c/K)}}\right)$$

$$\frac{1}{(k_1 - k_2)}\frac{dk}{dc} = \frac{1}{\sqrt{(1 + 4c/K)}} + \frac{k_2}{(k_1 - k_2)}$$

$$\frac{1}{(k_1 - k_2)}\frac{d^2k}{dc^2} = -\frac{1}{2}\frac{4/K}{(1 + 4c/K)^{3/2}} = -\frac{2}{K}\left(\frac{1}{\sqrt{(1 + 4c/K)}}\right)^3$$

$$\lim\left[\frac{d^2k/dc^2}{(k_1 - k_2)}\right]_{c=0} = -\frac{2}{K} \qquad (3)$$

APPENDIX II

Derivation of a rate equation follows which includes clustering of one of the reactants, B, in a bimolecular reaction. It is assumed that the second reactant, A, dissolves in the clusters to only a small extent. The fraction of B which clusters is assumed to follow an adsorption type equation and equals $1/(1 + a(B))$. The fraction which does not cluster is $1 - 1/(1 + a(B))$. If the total rate r equals $r_c + r_s$ where r_c is the rate for clusters and r_s is the rate for the more randomly distributed reactant, $r = r_c + r_s$.

$$r_s = k_s\,(A_s)(B)\,\frac{1}{1 + a(B)}$$

$$r_c = k_c\,(A_c)(B)\,\frac{a(B)}{1 + a(B)}$$

Assume that the amount of A in clusters, A_c, is much smaller than the amount of A in solvent, A_s; i.e., $A_c \ll A_s$. Assume further that A will distribute itself according to $(A_c) = k_3(A_s)$.

$$r = r_s + r_c = (A_s)(B)\left(k_s\,\frac{1}{1 + a(B)} + k_c k_3\,\frac{a(B)}{1 + a(B)}\right)$$

$$r = (A_s)(B)\frac{k_s + k_c k_3 a(B)}{1 + a(B)}$$

$$= (A_s)(B)k_s\frac{1 + \frac{k_c k_3}{k_s}a(B)}{1 + a(B)}$$

We might expect that $k_3 = 0$, deducing that if any A became associated intimately with clusters of B that reaction would ensue. But if in clustering, B combined with some solvent molecules, then perhaps some A could be dissolved in clusters without reaction occurring immediately, in which case $k_3 \neq 0$. This leads us to both positive and negative ester concentration effects, depending on the magnitude of k_3. The rate constant, k_c, would be expected to be very large because of the enhanced entropy factor of reactants so intimately associated. A simpler concept would be to recognize the increase in the magnitude of the concentration of B in clusters of B as compared to B as distributed more uniformly as it would be in the solvent. But arriving at the distribution of molecules in a non-regular solution is an enormous problem not to be solved in the near future. It would appear more practical to elucidate first the cruder aspects of clustering; i.e., whether they be large assemblages or small, of long or short duration.

APPENDIX III

Table 1

Summary of [TeaBr] and [Ester] effects in Acetone at 35.00°

Run	Salt (mM)	$k_{xpt.}$ ($1/10^3$ min.)	$1/k_{xpt.}$ (min.)	Ester (M)	H_2O (M)
S25	1.48	18.4	54.4	0.26E	
S26		16.4	61.0	0.52E	
S27		19.9	50.2	0.13E	
S44	2.37	28.3		0.27E	
S45		28.5		0.26E	
S46	1.381	17.93			
S47	0.595	8.43			
S48	0.119	1.62			
S49	0.275	4.01			
S50	1.975	23.6			
S54	2.26	21.9	45.6	1.00E	.00855
S55		13.8	72.5		.173
S56		17.2	58.0		.0865
S73	2.89	30.9	32.4	0.24G	
S74		32.8	30.5	0.11G	
S75		4.66	214	0.11C	
S76		4.77	210	0.09C	
S77		30.2		0.26E	

Table 2

Summary of [TeaBr] [TbaBr] and [Ester] Effects in Acetone at 25.00°

Run	Salt (mM)	$k_{xpt.}$ ($1/10^3$ min.)	$1/k_{xpt.}$ (min.)	Ester (M)
	TeaBr			
S57	2.32	11.16		0.26E
S58	5.82	24.6		
S59	0.586	2.9		
S60	1.45	7.31	137	
S61		7.70	130	0.10E
S62		6.45	155	0.24G
S63		7.53	133	0.12G
S64		.816	1225	0.24C
S65		1.046	957	0.12C
S66	4.38	18.86		0.26E
S67	2.90	13.53		
	TbaBr			
S68	6.76	28.2		0.26E
S69	27.2	91.3		
S70	2.75	13.1 ± .2		
S71	13.6	30.2		
S72	10.9	24.0		

Table 3

Summary of [TeaBr] and [Ester] Effects in Acetonitrile at 35.00°

Run	Salt (mM)	$k_{xpt.}$ ($1/10^3$ min.)	$1/k_{xpt.}$ (min.)	Ester (M)
A2	9.21	6.89		0.13E
A3	3.96	3.24		
A4	19.7	14.9		
A5	39.6	31.0		
A6	29.7	23.3 ± .4		
A7	15.6	12.3	81.4	0.52E
A8		12.5	80.0	0.26E
A9		12.7	78.8	0.13E
A22	44.7	25.1	39.8	0.12G
A23		26.3	38.0	0.19G
A24		4.82	208	0.09C
A25		5.15	194	0.11C

Table 4

Summary of [TeaBr] and [Ester] Effects in Acetonitrile at 25.00°

Run	Salt (mM)	$k_{xpt.}$ ($1/10^3$ min.)	$1/k_{xpt.}$ (min.)	Ester (M)
A10	6.85	2.04		0.13E
A11	3.41	1.025		
A12	71.9	20.6 or .7		
A14	16.7	5.25		0.26E
A15		5.30		0.13E
A16	28.6	8.48		0.39E
A17		8.49		0.26E
A18		1.27		0.24C
A19				0.12C
A20		6.36		0.24G
A21				0.12G

Table 5

Summary of [TeaBr] and [Ester] Effects in Nitromethane at 35.00°

Run	Salt (mM)	$k_{xpt.}$ ($1/10^3$ min.)	$1/k_{xpt.}$ (min.)	Ester (M)
N2	2.35	0.863		0.26E
N3	5.86	2.20		
N4	4.40	1.666		
N5	2.93	1.099		
N6	5.90	2.02		
N7	19.0	6.33		
N8	8.90	3.80		
N9	39.2	14.71		
N10	5.74	2.15		
N11	19.0	7.27	138	
N12		7.59	132	0.13E
N13		7.21	139	0.49E
N23	71.1	20.1	49.7	0.12G
N24				0.21G
N25		3.84	260	0.12C
N26		4.1	244	0.074C

Table 6

Summary of [TeaBr] and [Ester] Effects in Nitromethane at 25.00°

Run	Salt (mM)	$k_{xpt.}$ ($1/10^3$ min.)	$1/k_{xpt.}$ (min.)	Ester (M)
N14	73.6	10.23		0.13E
N15	147.9	21.2		
N17	73.6	10.35		
N18	71.0	1.49		0.24C
N19		7.54		0.24G
N21		7.50		0.12G
N22	107.1	2.22		0.12C

Table 7

Ester Concentration Effect Constants

Entries are b x molarity where $k = k_o/(1 + b(\text{ester}))$.

Ester	Temp.	Acetone	Acetonitrile	Nitromethane
E	35°	0.35	0	0
	25°	0.60	0.09	0.14
G	35°	1.61	0	0
	25°	0.48	-0.56	0
C	35°	3.31	0	0
	25°	0.94	-2.46	1.60

Table 8

Second-Order Rate Constants

Entries are k_{ol}(min. x molarity) = $k_o/(Br^-)$ x 10^3)

Ester	Temp.	Acetone	Acetonitrile	Nitromethane
E	35°	16.7	0.80	0.40
	25°	6.0	0.30	0.143
G	35°	15.4	0.52	0.28
	25°	6.7	0.22	0.106
C	35°	2.3	0.085	0.064
	25°	1.10	0.044	0.021

Table 9

Enthalpies of Activation

Entries are $\Delta H^{\ddagger}$/kilocal.

Ester	Acetone	Acetonitrile	Nitromethane
E	18.9	18.0	18.8
G	15.3	16.0	18.0
C	14.7	12.1	20.4

$$\Delta H^{\ddagger} = Rd(\ln k_{ol})/d(1/T) = (R/\Delta(1/T))\,\Delta\ln k_{ol}$$

$$T_2 - T_1 = 10^{\circ}\ \Delta(1/T) = -0.000108$$

$$\Delta H^{\ddagger} = -(1.987 \times 10^{-3}/0.000108)\ \Delta\ln k_{ol}$$

$$= -18.4\ \Delta\ln k_{ol}\ \text{kilocal.}$$

Table 10

Entropies of Activation

Entries are $\Delta S^{\ddagger}$/cal.

Ester	Acetone	Acetonitrile	Nitromethane
E	+ 0.3	- 8.7	- 7.6
G	-11.6	-16.1	-10.8
C	-17.4	-32.3	- 6.0

$$k_{ol} = (k'T/h) \exp(-\Delta H^{\ddagger}/RT) \exp(\Delta S^{\ddagger}/R)$$

$$\ln k_{ol} = \ln(k'T/h) - (\Delta H^{\ddagger}/RT) + \Delta S^{\ddagger}/R$$

$$\Delta S^{\ddagger} = \Delta H^{\ddagger}/T + R \ln k_{ol} - R \ln(k'T/h)$$

$R\ln(k'T/h)$ = 58.61 cal. at 35°, 58.54 cal. at 25°

The unit of time for k_{ol} is seconds here.

APPENDIX IV

Table 11

Some Properties of the Solvents (16)(21)(29)(28)

	Acetone	Acetonitrile	Nitromethane
30°			
D^+	20.2	35.6	35.9
$(T/\theta_c)^+$	1.43	1.63	1.32
μ gas	$2.89\ 10^{-8}$ esu.	$3.96\ 10^{-8}$ esu.	$3.44\ 10^{-8}$ esu.
d	0.7793 g./ml.	0.7714 g./ml.	1.1245 g./ml.
	0.295 cp.	0.325 cp.	0.595 cp.
	22.01 dyne/cm.	27.80 dyne/cm.	35.51 dyne/cm.
vp.	282.5 mm.	111.8 mm.	47.6 mm.
N.B.P.	56.2°	81.6°	101.2°
$\Delta H_{25°}$	7650 cal/g.mole	8530 cal/g.mole	8250 cal/g.mole
25°	9.8	12.3	12.6

+An empirical equation (43) $D = D_{T_o} \exp(-(T - T_o)/\theta_c)$ has been used to correlate data of D vs. T. Note that ΔF of a solvent attending the removal of ions from it equals $-c(1/D)$ while $T\Delta S$ for this change equals $cT(d/dT)(1/D) =$

Table 11 (cont.)

$c(T/\theta_c)(1/D)$. In other words, if $(T/\theta_c) \geq 1$ as it is for the three solvents used here, the solvent will withdraw heat from an isothermal bath for this process or tend to cool. This can be interpreted in terms of the relative difference in molecular motions between pure solvents with and without ions in them. The solvent with the larger T/θ_c is the solvent whose molecular motions are most suppressed by the attractive fields of ions. That solvent will consequently have a greater tendency to form non-regular solutions with ions. We can extend the treatment to include dipolar solutes and conclude that of the three solvents used in this work acetonitrile would be most likely to form non-regular solutions. Indeed, it was in acetonitrile that the most confusing change of rate constants with ester concentration were noted.

Table 12

Some Properties of the Esters

	Succinate	Glutarate	Caproate
d^{+}	1.46 ± 0.01	1.42 ± 0.02	1.24 ± 0.02
d^{++}	1.512 at 25°		
B.P.	53 - 56°/50μ	ca.60°/ca.25μ	below 35°/0.5mm.

d is given in units of g./ml.

[+]Densities of freshly dried esters were roughly determined at room temperature using a syringe to deliver an approximate volume and an analytical balance to weigh.

[++]Before the sensitivity of esters to water was appreciated, this precision value of succinate was established for material which had been dried and then exposed to room air.

Table 13

Comparison of Second-order Rate Constants with those of Frashier

	k_{ol} x molarity x 10^3 min.	K	Salt
35°	16.7	15 x 10^{-3}	TeaBr
(Frashier)	15.03	3.6 x 10^{-4}	LiBr
25°	6.0	8 x 10^{-3}	TeaBr
(Frashier)	6.32(24.9°)	3.6 x 10^{-4}	LiBr
ΔH mole/kilocal.	18.9	15.66	

Table 14

List of Symbols and Abbreviations

A	Acetonitrile
a	Ester concentration effect constant
b	Frashier's ester concentration effect constant
C	Caproate, methyl α-bromoisocaproate
c	Gross salt concentration, a constant in Table 11
D	Dielectric constant
E	Succinate, dimethyl α-bromosuccinate
E	(superscript) Excess thermodynamic quantity
$\Delta F^{\ddagger}$	Free energy of activation
G	Glutarate, dimethyl α-bromoglutarate
g	Kirkwood's dipole interaction factor
$\Delta H^{\ddagger}$	Enthalpy of activation
h	Planck's constant
K	Equilibrium constant
k	Pseudo first-order rate constant = $-(1/2)(\Delta \ln a/\Delta t)$
k_1	Second-order rate constant for bromide ion
k_{o1}	Bromide ion second-order rate constant extrapolated to zero ester concentration
k'	Boltzmann's constant
M	Molarity
mM	Millimolarity

R	Perfect gas constant
r	Reaction rate
r_s	Reaction rate in the solvent
r_c	Reaction rate in clusters
S	Acetone
T	Temperature
t	Time in minutes, seconds in Table 10 only
α	Optical rotation
γ	Surface tension, activity coefficient
δ	Solubility parameter
	Viscosity
θ	Angular reading
θ_o	Zero angular reading
μ	Micron Hg pressure, dipole moment
ca.	Approximately
NBP	Boiling point at one atmosphere
TeaBr	Tetraethylammoniumbromide
TbaBr	Tetrabutylammoniumbromide
vp.	Vapor pressure

APPENDIX V

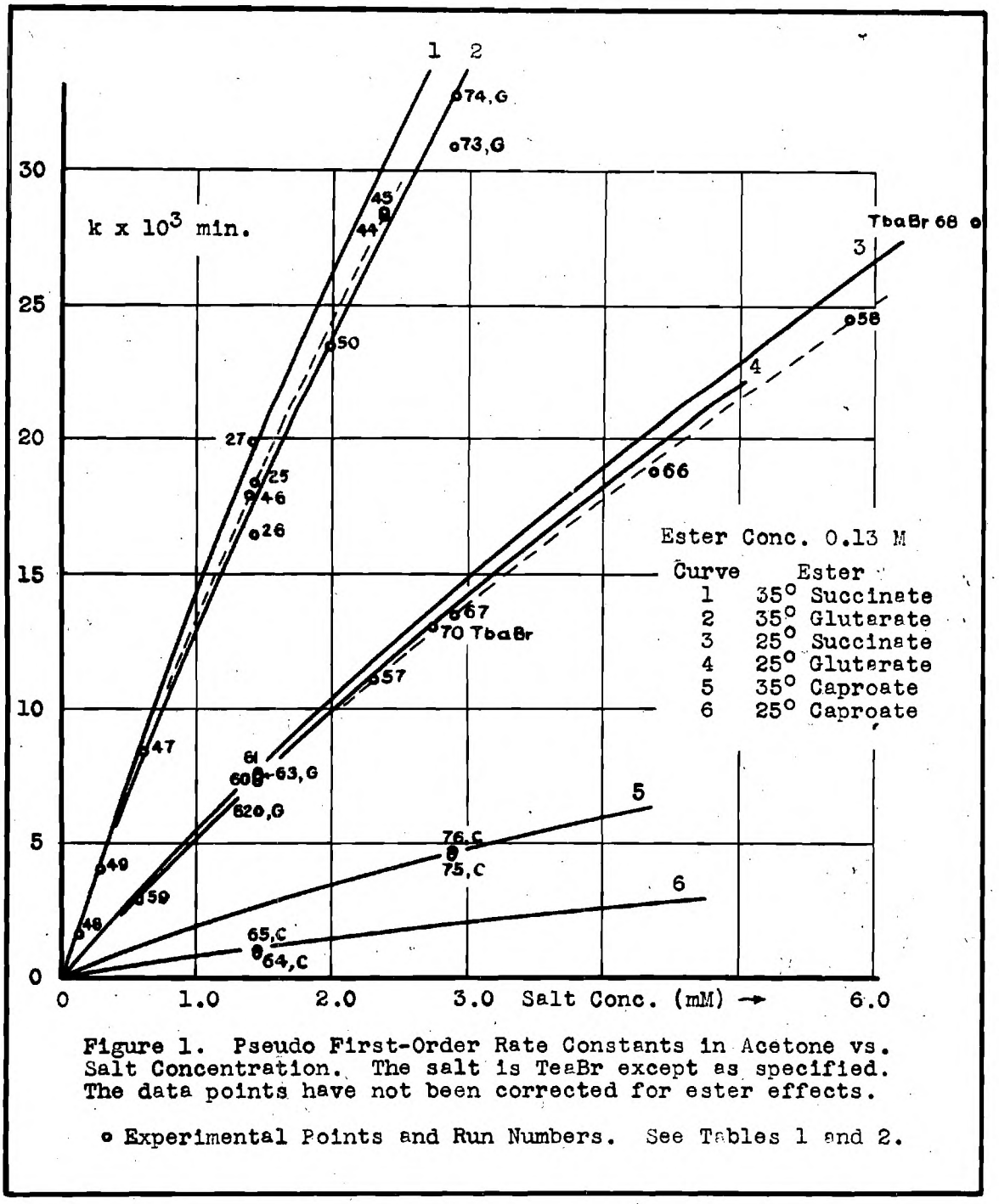


Figure 1. Pseudo First-Order Rate Constants in Acetone vs. Salt Concentration. The salt is TeaBr except as specified. The data points have not been corrected for ester effects.

o Experimental Points and Run Numbers. See Tables 1 and 2.

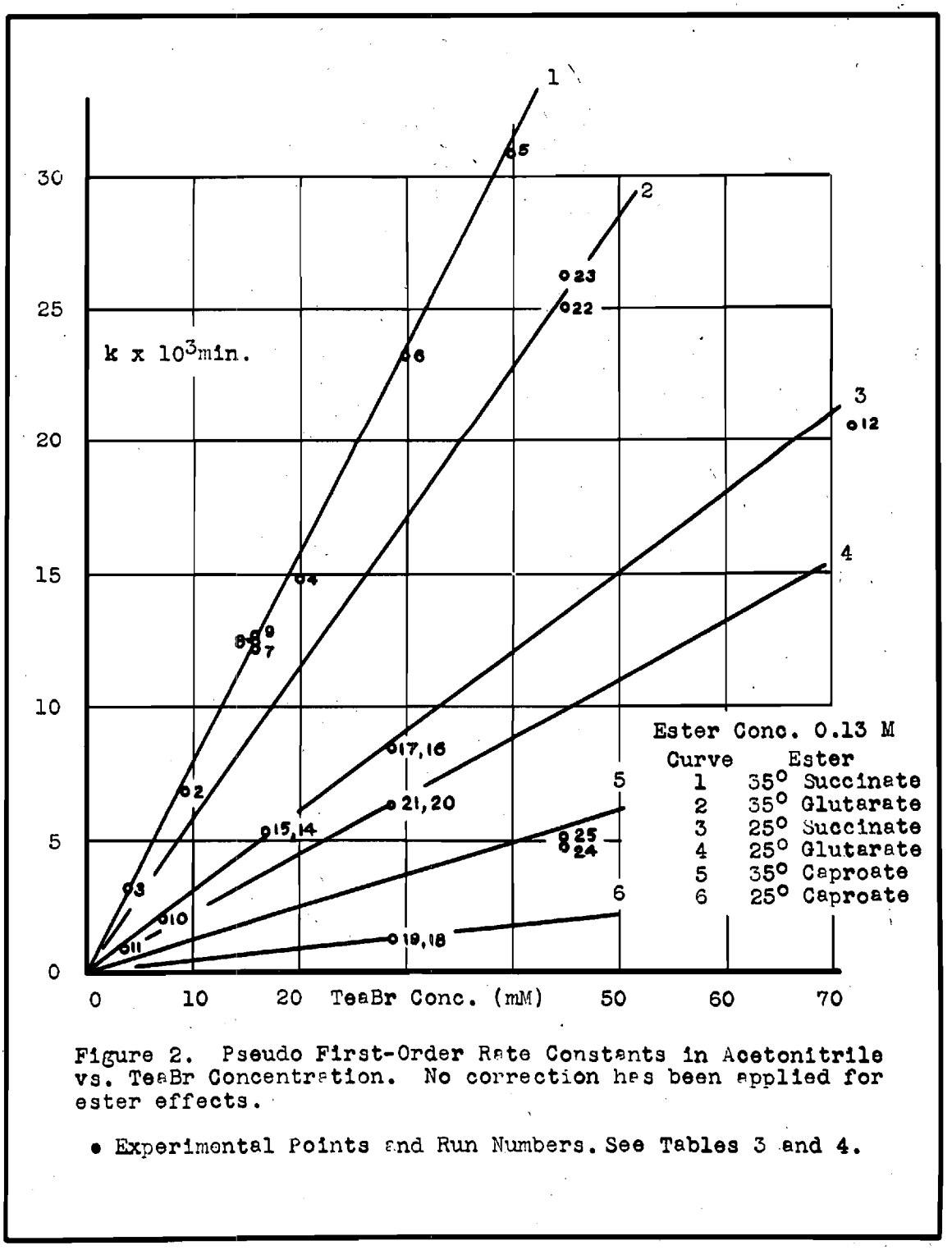


Figure 2. Pseudo First-Order Rate Constants in Acetonitrile vs. TeaBr Concentration. No correction has been applied for ester effects.

• Experimental Points and Run Numbers. See Tables 3 and 4.

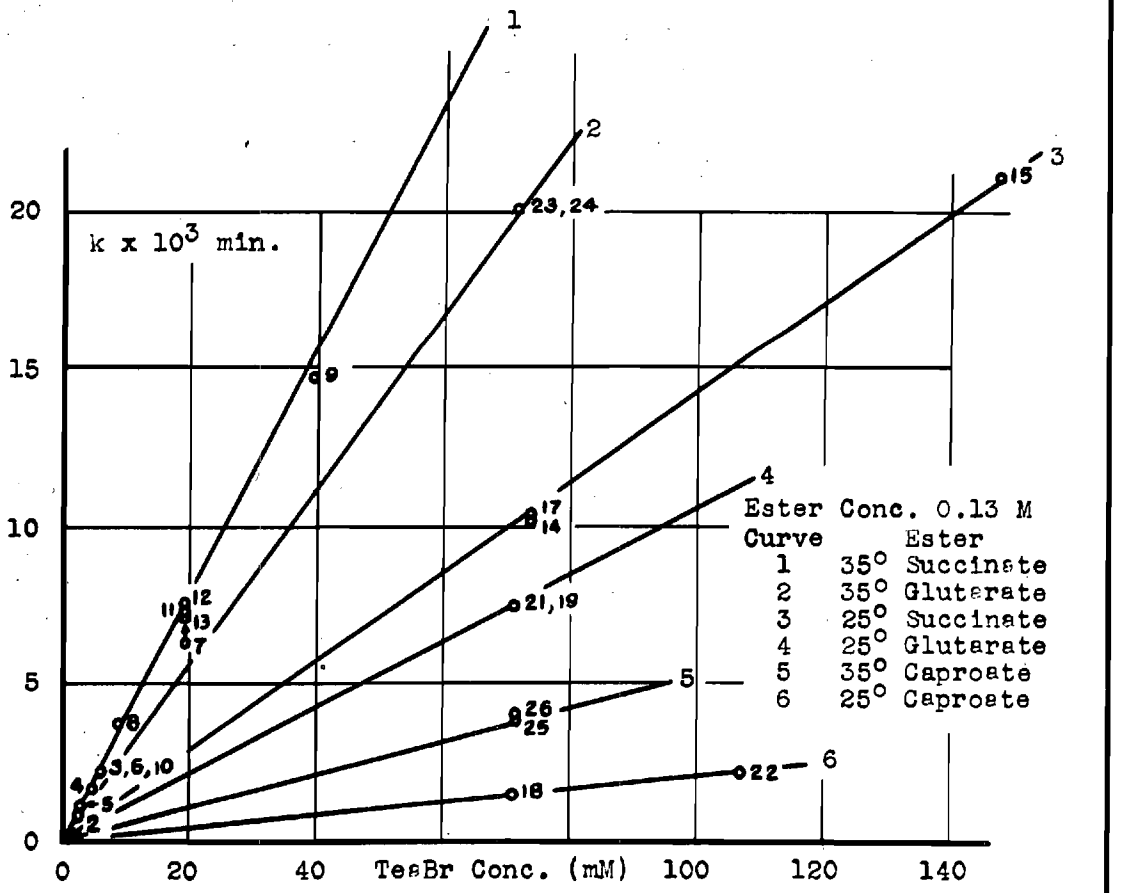
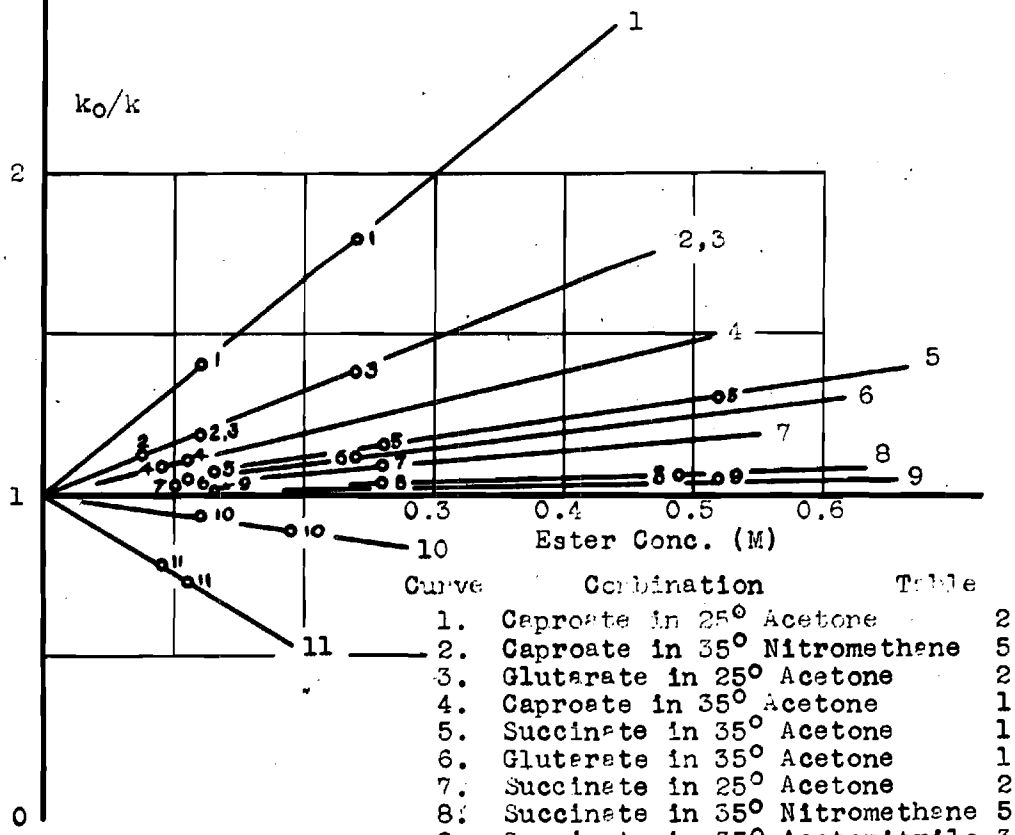


Figure 3. Pseudo First-Order Rate Constants in Nitromethane vs. TeaBr Concentration. The data points have not been corrected for ester effects.

• Experimental Points and Run Numbers. See Tables 5 and 6.



Curve	Combination	Table
1.	Caproate in 25° Acetone	2
2.	Caproate in 35° Nitromethane	5
3.	Glutarate in 25° Acetone	2
4.	Caproate in 35° Acetone	1
5.	Succinate in 35° Acetone	1
6.	Glutarate in 35° Acetone	1
7.	Succinate in 25° Acetone	2
8.	Succinate in 35° Nitromethane	5
9.	Succinate in 35° Acetonitrile	3
10.	Glutarate in 35° Acetonitrile	3
11.	Caproate in 35° Acetonitrile	3

• Experimental Points with Curve Numbers

Figure 4. Ester Concentration Effect on Rate Constant

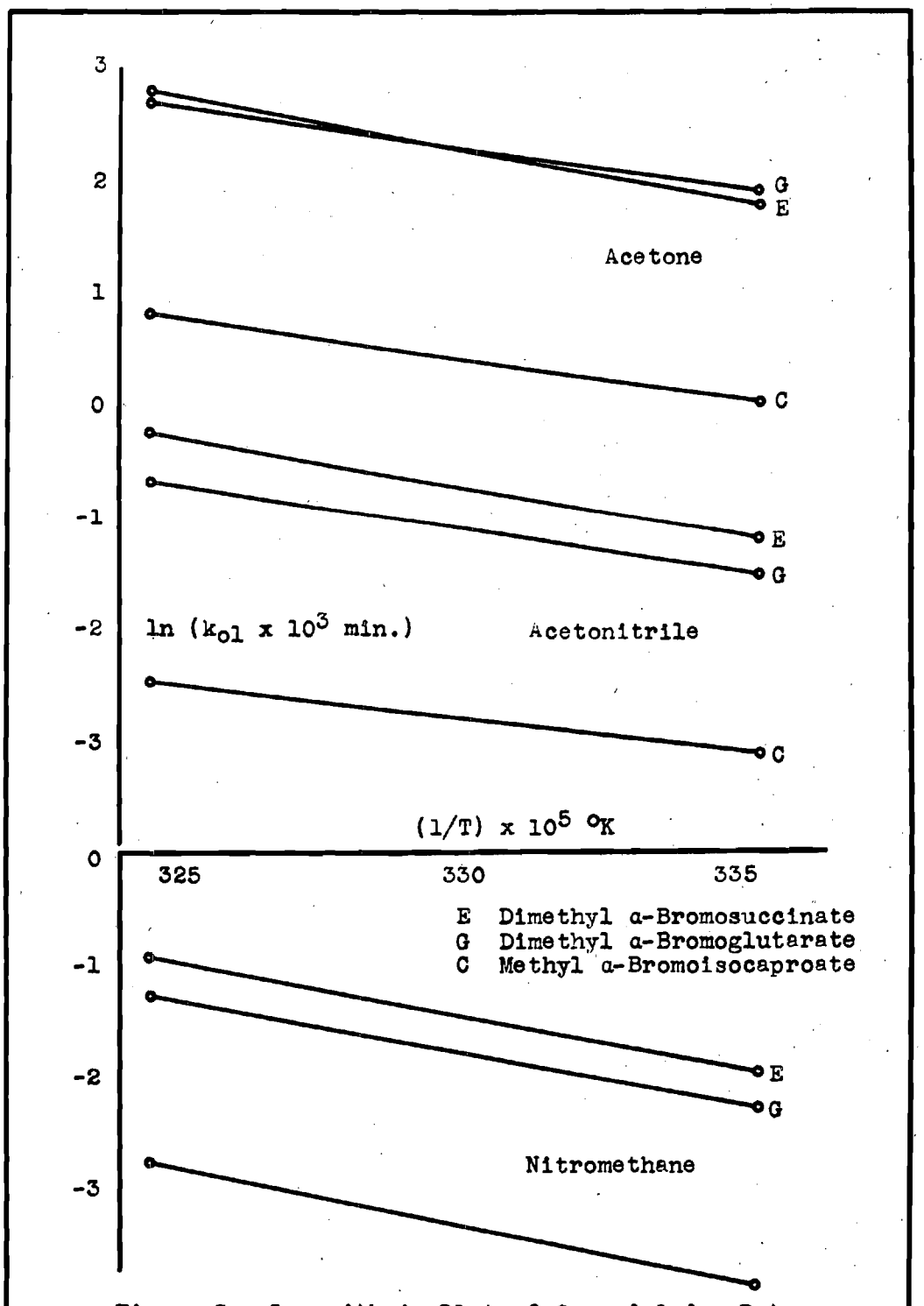


Figure 5. Logarithmic Plot of Second-Order Rate Constant for Bromide Ion vs. Reciprocal Temperature.

Experimental Points. See Table 8.

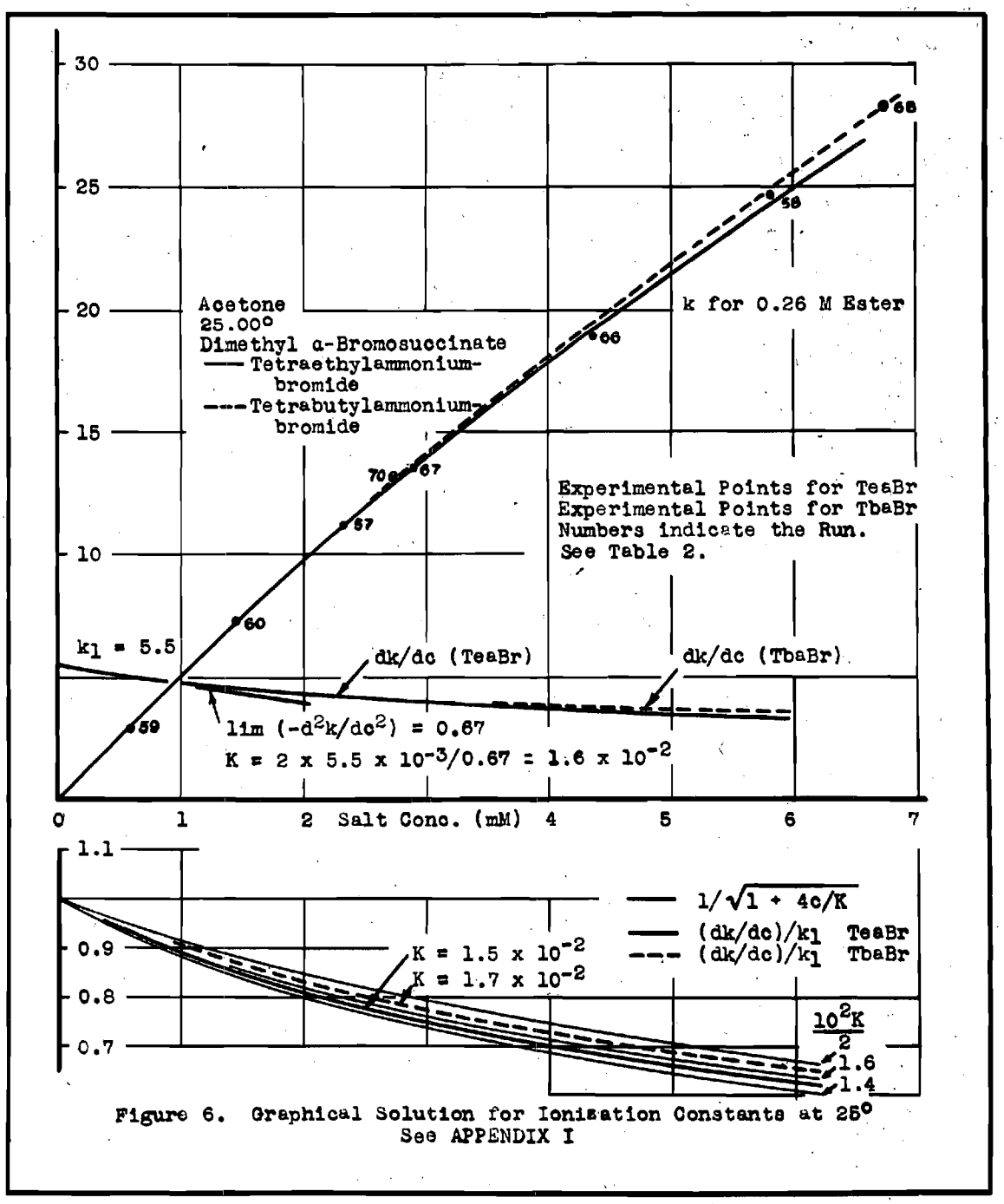


Figure 6. Graphical Solution for Ionisation Constants at 25°
See APPENDIX I

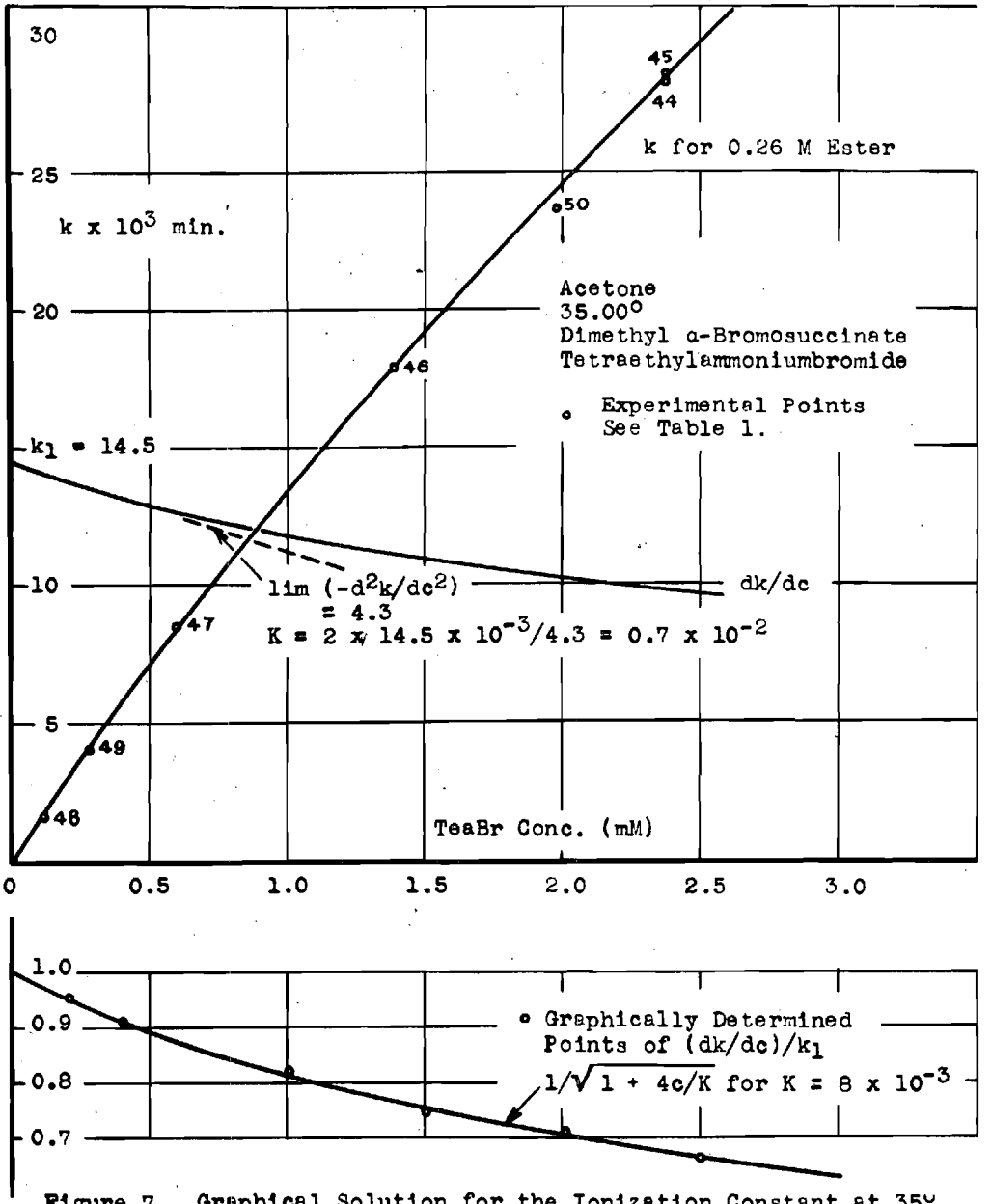


Figure 7. Graphical Solution for the Ionization Constant at 35°
See APPENDIX I

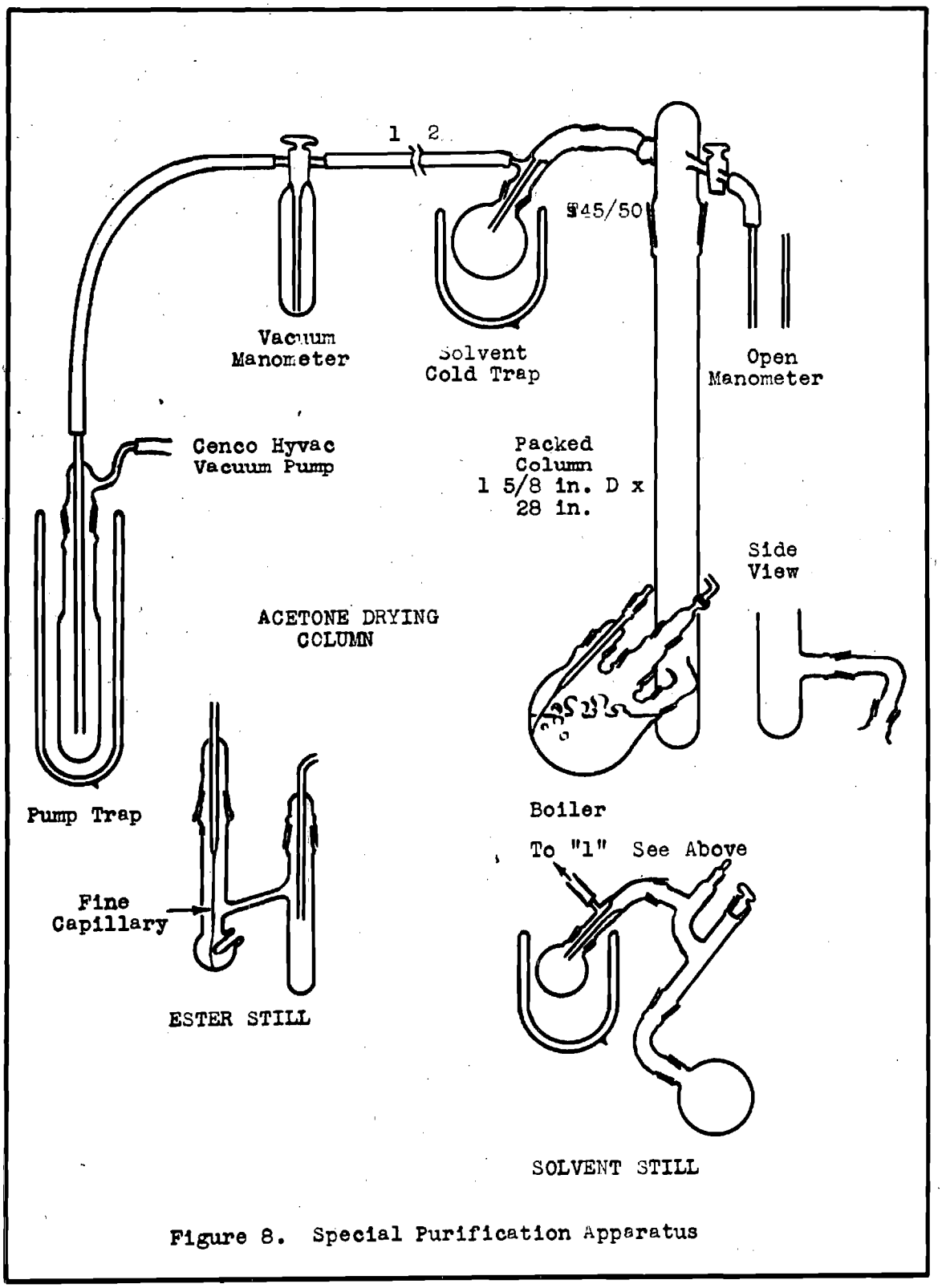


Figure 8. Special Purification Apparatus

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VITA

Lyman Wallace Morgan was born in Okmulgee, Oklahoma on March 1, 1924. He attended elementary school and high school in Muskogee, Oklahoma, graduating in 1941. Entering the Massachusetts Institute of Technology with a Freshman Competitive Scholarship, he stayed two years before being called into active duty with the Army of the United States in June, 1943. He served in the Army Signal Corps in India and China as a radio transmitter repairman, having the rank of staff sergeant, technician. He was commissioned Second Lieutenant in the Chemical Corps of the U. S. Army Reserve in May, 1949.

After reentering the Massachusetts Institute of Technology in 1946, he graduated in 1948 with a Bachelor of Science degree in Chemical Engineering. His thesis was on the compressible flow of perfect gases.

The following Fall, he entered the Georgia Institute of Technology with a Teaching Assistantship in Chemical Engineering. The next year a Research Fellowship was received to perform a pilot plant study of the fluidized distillation of sawdust with Mr. George M. Armstrong, Jr. under the direction of Dr. H. C. Lewis. The following year he entered the School of Chemistry with a Teaching

Assistantship to prepare for a Ph. D. in Physical Chemistry under the direction of Dr. Loyd D. Frashier. On March 18, 1951 he married Miss Evelyn Louise Garrison of Fredericksburg, Virginia. In April, 1951 a paper on the sawdust distillation was delivered by Mr. Armstrong and himself at a Regional American Institute of Chemical Engineers Meeting in Atlanta, Georgia. He received the Masters Degree in Chemical Engineering June, 1951.

Each summer during the years he worked on his Ph. D. program he was associated with his father, R. D. Morgan, in the milk and ice cream business in Muskogee, Oklahoma. In June of 1954 he joined his father and continued with the business until September of 1955. At that time, he accepted an Instructorship in Physical Chemistry at Oglethorpe University in North Atlanta, Georgia, and taught there while writing his Ph. D. thesis.

In January, 1956 he accepted an offer in the Research and Development Department of the Phillips Petroleum Company, Bartlesville, Oklahoma as a Systems Engineer. In this position he designs tests for the controllability of pilot plant and full scale chemical processes and studies the theoretical and simulated behavior of controlled systems. His family, including two girls, resides in Bartlesville. He belongs to the American Institute of Chemical Engineers, the American Chemical Society, and the Society of Sigma Xi.